Developmental effects on reproductive hormone levels:

A migrant study

Alejandra Núñez-de la Mora

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ABSTRACT

Previous studies have established that average profiles of salivary progesterone and oestradiol, differ considerably among populations. Diet, age, and energetics appear responsible for acute inter-populational differences, but significant, unexplained differences in chronic levels of reproductive steroids remain. Based on developmental hypotheses advanced by reproductive ecologists, a migration study was initiated to assess whether environmental conditions experienced during development can influence patterns of adult ovarian hormones. Salivary steroid profiles of Bangladeshi women who migrated to the UK at different times (infancy, childhood, adulthood) were compared to those of women in Bangladesh, second-generation Bangladeshi migrants, and white women born and resident in the UK. Data on socio-demographics, anthropometry, physical activity, diet and reproductive history were also collected. The following hypotheses and predictions were examined: A) Early life conditions influence adult set points of ovarian steroid hormones -- women in Bangladesh and adult migrants will have lower ovarian steroids than child migrants, second generation and white women; B) improved conditions during childhood can alter levels of ovarian steroids -- child migrants will have levels of ovarian steroids that are negatively correlated with age at migration; and C) alterations in conditions after maturation do not modify set points established during early life -- adult migrants will have steroid levels that are comparable to Bangladeshi sedentees. The predictions were upheld for progesterone but not for oestradiol. Results point to infancy and childhood as a sensitive period when changes in environmental conditions determine the tempo of growth and maturation, as well as later adult progesterone levels. In contrast, no evidence was found of a developmental effect on adult levels of oestradiol. The alterations in hormones levels among Bangladeshi migrants, together with a changing diet and reproductive behaviours, may put child migrants and second-generation women at increased risk for breast cancer in later life.

To my parents,

Alicia and Gabriel

Author's declaration

I declare that the work in this dissertation was carried out in accordance with the Regulations of University College London. The work is original, except where indicated by special reference in the text, and no part of the dissertation has been submitted for any other academic award. Any views expressed in this dissertation are my own and not those of the University.

Alejandra Núñez-de la Mora

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PREFACE

Over the past two decades, pathbreaking studies by reproductive ecologists have established that levels of ovarian function, measured as average profiles of salivary progesterone and oestradiol, vary considerably among populations (Ellison *et al.*, 1986; Danutra *et al.*, 1989; Bailey *et al.*, 1992; Ellison *et al.*, 1993a; Panter-Brick *et al.*, 1993; Jasienska & Ellison, 1998; Vitzthum *et al.*, 2002). It is well established that constitutional and acute ecological factors such as age and energy balance are responsible for some of this variance (Lipson & Ellison, 1992; Ellison *et al.*, 1993b; O'Rourke & Ellison, 1993; Ellison, 1995). However, even after these factors are accounted for, significant inter- and intra-population differences in ovarian function remain, of which neither the significance nor the aetiology are well understood.

Recent hypotheses (Ellison, 1990, 1996; Worthman, 1999; Lipson, 2001) have incorporated developmental issues to explain such variance and propose that adult levels of ovarian hormonal function are associated with the tempo of childhood and adolescent growth and maturation. This implies that varying levels of reproductive hormones in later life result from differences in environmental conditions encountered during development.

The aim of this study was to test this developmental hypothesis empirically by studying women who, as a result of migration have experienced discontinuous environmental conditions at different stages of their life cycle. The effect of different formative environments on adult levels of ovarian hormonal function was examined by comparing salivary steroids in three different migrant groups and two reference groups. The changes in nutrition, lifestyle and reproductive variables experienced by migrants were assessed through detailed questionnaires.

Migrant groups

1) First generation Bangladeshi migrants who spent their infancy and childhood in Sylhet, Bangladesh but moved to the UK as adolescents or adults.

2) First generation Bangladeshi migrants who spent their infancy in Sylhet, Bangladesh but moved to the UK as young children.

3) Second generation Bangladeshi migrant women who were conceived, born and raised in the UK but whose parents moved from Sylhet, Bangladesh to the UK.

Reference groups

1) Women living in Sylhet, NE Bangladesh who were born and raised there.

2) Non-Bangladeshi, white women living in similar neighbourhoods as the immigrant Bangladeshis in London, whose parents and at least both grandmothers were born in the UK.

The hypotheses tested were:

Poor environmental conditions experienced during infancy and childhood will result in adult women having lower average baseline levels of ovarian steroid hormones (progesterone and oestradiol) than those living in more affluent conditions. Prediction A: Sylheti women and adult migrants will have lower ovarian steroids than child migrants, second generation women and white women.

A positive change in environmental conditions that impacts developmental tempo will be reflected in enhanced reproductive hormonal function; thus, migrants who move to an affluent environment while growth and development is ongoing, will have higher ovarian

steroid levels than sedentees. Prediction B: Child migrants will have levels of ovarian steroids that are negatively correlated with pre-pubertal age at migration.

Alterations in conditions after maturation will not modify the set points established during early life. Prediction C: Adult migrants will have steroid levels that are comparable to Sylheti sedentees.

The Bangladeshi community in London was chosen for the migrant population for several reasons:

1) Bangladesh is one of the poorest nations in the world with a low GNP, a low life expectancy, the highest international rate (39%) for low birth weight babies (< 2500g), and with approximately 47% of the population living below the poverty line (World Bank, 2003; http://www.unu.edu/unupress/food2/UID03E/uid03e06.htm). From a developmental viewpoint, these statistics contrast enormously with conditions in the UK. For instance, Bangladesh's per capita GNP is a mere 1.4% that of the UK, life expectancy for women is a third shorter and the prevalence of low birth weight 5 times higher than in the UK (see Table 13 in Chapter 5 for more detailed comparisons).

2) Previous studies in both urban and rural Bangladeshi women have identified significantly lower levels of reproductive hormones compared to those of Western healthy women (Seaton & Riad-Fahmy, 1980; Brindle *et al.*, 1988; Holman *et al.*, 1995; Rahman, 1996; Núñez-de la Mora, 2000; Núñez-de la Mora *et al.*, 2002; O'Connor *et al.*, 2003), which confirms that native Bangladeshi women and white UK women are appropriately contrasted populations.

3) Bangladeshis in the UK constitute a multi-generational population that allows for recruitment of individuals who entered Britain at different life stages (infancy, childhood, adulthood) (Champion, 1996; Haskey, 1997).

4) Ninety-five percent of these migrants originate from a single geographical region (Sylhet District) (Carey & Shukor, 1985; Eade *et al.*, 1996a) and have very low intermarriage with other ethnic groups in England (Berrington, 1996). These two factors arguably reduce "genetic" noise.

5) Immigrant Bangladeshis are relatively homogeneous in socio-economic terms and share similar histories of migration (Carey & Shukor, 1985; Eade *et al.*, 1996a). This facilitates the analysis of independent variables.

The thesis is divided into three sections:

Section I deals with various social and behavioural aspects of this research:

Chapter 1 provides background information on the study design and methodology used.

Chapter 2 provides an overview of the history and background of the Bangladeshi community in the UK and reports on socio-demographic trends among migrants in comparison to the reference groups.

Chapter 3 provides background information on the practice of betel nut chewing in the Bangladeshi community, with special reference to cross- generation comparisons among Bangladeshi women.

Section II deals with aspects related to the hormonal measurements:

Chapter 4 presents the results of a pilot study that was undertaken to evaluate the effects of chewing betel quid on the accurate measurement of salivary steroids. Since many Bangladeshi women

regularly chew betel nut, it was necessary to assess the practicability of using salivary immunoassay techniques in this population.

Chapter 5 presents the hormonal results vis-à-vis the predictions of the developmental hypothesis for variation in ovarian function.

Section III deals with the public health implications of the hormonal, social and behavioural data collected during the study:

Chapter 6 analyses changes in diet, activity, anthropometric and reproductive variables among Bangladeshi migrants in the context of breast cancer risk factors to illustrate how changes brought about by migration may impact health in this community.

Candidate's contribution

In partnership with Dr. Gillian R. Bentley, the candidate was fully involved in all stages of the present research, including the pilot study: ANM participated in the designing of the experimental strategy, the networking with the Bangladeshi community both in Sylhet and London, and the organisation and logistics of fieldwork; wrote several funding applications of which three were successful in financing part of the study; designed and piloted both questionnaires; ran most of the informative workshops on reproductive health at the participating community centres where recruitment was carried out; coordinated the research assistants during the recruitment and follow-up processes and conducted all the interviews and saliva collection in Bangladesh and 80% of those in the UK; performed the totality of the radioimmunoassays in the laboratory and was responsible for coding, entering and rectifying the questionnaire and hormonal data; she undertook all the data and statistical analyses, as well as the interpretation, discussion and writing of the results.

CHAPTER 1

STUDY DESIGN AND METHODOLOGY

Migrant studies: uses, advantages and limitations

Almost a century ago Boas (1912) developed the strategy of using migration studies to estimate the degree of human plasticity and to help partition the components of adaptation, particularly to discriminate between genetic adaptation and developmental adaptability. Since then, migration studies have been used as natural experimental models to assess the impact of diverse environments (biological and social) on certain aspects of the phenotype (Lasker, 1969; Lasker & Mascie-Taylor, 1988; Lasker, 1995). By comparing migrants with non-migrants of identical (or at least similar) genotypes, research has focused on which aspects of the phenotype (growth (Shapiro, 1939; Goldstein, 1943; Lasker, 1954; Goel *et al.*, 1981; Bogin *et al.*, 2002)) and development (Proos *et al.*, 1991b), fertility (Schoenmaeckers *et al.*, 1999), physiology, general health, dietary (Landman & Cruickshank, 2001), reproductive (Leidy, 1998) and other behaviours (Cantor-Graae & Selten, 2005), etc.) change after migration, and in identifying factors in the new environment that are responsible for those changes. Factors assumed to be different are many and varied and they include: qualitative and quantitative changes in diet and levels of physical activity, availability of health care and public services, socio-economic and demographic variables, exposure to pollutants and pathogens, and ecological variables such as altitude, temperature, radiation and humidity.

Migration studies have aided research on the effects of urbanisation, modernisation and westernisation, in particular in the context of the nutritional and epidemiological transitions (Ostby *et al.*, 1989; Salmond *et al.*, 1989; Dufour & Piperata, 2004). Such studies have been

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invaluable in shedding light on to the effects of behavioural and biosocial cultural practices on disease risk. In particular, Type 2 diabetes mellitus (Gerber, 1984; Serrano-Rios *et al.*, 1999; Misra & Vikram, 2004), obesity (Ramirez & Mueller, 1980), hypertension (James *et al.*, 1985; Agyemang *et al.*, 2004), cancer (Modan, 1980; Shimizu *et al.*, 1991; Ziegler *et al.*, 1993; Liao *et al.*, 2003; Smith *et al.*, 2003a), cardiovascular disorders (McKeigue *et al.*, 1988) and asthma (Rottem *et al.*, 2005).

Migrant studies have also contributed to the notion that plasticity of some anthropometric measurements is restricted to certain windows during development. Specifically, these studies have shown that the effects of improved conditions on skeletal growth are dependent on the age at which migration occurs (Shapiro, 1939).

One of the main strengths of migrant study designs is that they permit the partitioning of the components of adaptation, particularly the discrimination between genetic adaptation and developmental adaptability. They provide an alternative to longitudinal studies to assess developmental effects, and in practical terms, conducted as cross-sectional designs, they can prove considerably less expensive and time-intensive, easier to implement and potentially more cost effective than their long-term counterparts. However, migrant designs are not without limitations. One major problem lies in determining which from a complex array of environmental variables that differ between the donor and recipient localities is responsible for effects found in the biological comparison of migrants and sedentees. Another limitation refers to the need to assess and control for variation due to selective migration, where migrants can differ from non-migrants in a number of biological traits due to the fact that immigrants are not necessarily a random sample of the population represented by the sedentees. Careful experimental design can help ameliorate such limitations (Lasker, 1952, 1954).

Capitalising on the advantages of a cross-sectional approach, a migrant study design was chosen as an appropriate strategy to address the question of the developmental effects on reproductive hormones that is the focus of this dissertation.

Sample characteristics

Study volunteers were healthy women of reproductive age (19 – 39 yr) who were divided into five groups according to their place of birth and where it applies, age at migration into the UK. The assumption was that women in each of the study groups would have experienced contrasting environmental conditions during different phases of their lifecycle.

As outlined in the Preface, the five groups under consideration were:

1) Bangladeshi women living in Sylhet who were born and raised there (SYL).

2) First generation migrants who spent their infancy and childhood in Sylhet but moved to the UK as adults (post-menarche) (ADU).

3) First generation migrants who were born in Sylhet but moved to the UK as infants or children (pre-menarche) (CHI).

4) Second generation migrant women who were conceived, born, and raised in the UK but whose parents moved from Sylhet to the UK (2ndGEN).

5) Non-Bangladeshi, white women living in London whose parents, and at least both grandmothers, were born in the UK (WHI).

(The abbreviations in brackets are the labels that will identify each group henceforth)

Sample size and compliance

A total sample size of 250 women with 5 sub-groups was targeted following a compromise a priori power analysis for ANOVA (using

G*Power) (psycho.uniduesseldorf.de/aap/projects/gp/power/index.html,)
with a specified significance value (α = 0.05), power (1-ß =0.95), and a
conventional "medium" effect size (Cohen's "f" = 0.28, adjusted from
0.25). Multiple regressions for a medium effect size (Cohen's "f2" =
0.15), require an even smaller total sample size of 138.

The aimed sample size of 50 participants in each study group, was
completed and even exceeded for all groups except for the second
generation group, for which only 34 women were recruited. At the end of
the study the total number of participants in the study was 249 (Sylhet
sedentees = 52, Adult migrants = 62, Child migrants = 51, Second
generation women = 34 and White women = 50). However, attrition of
the sample due to menstrual cycle irregularities, incomplete collections,
insufficient saliva sample volume and technical problems in the
laboratory resulted in a smaller sample size (n = 227) for hormonal
analysis (Sylhet sedentees = 48, Adult migrants = 56, Child migrants =
42, Second generation women = 33 and White women = 48). Detailed
sample sizes for each hormone are detailed in Chapter 4.

Compliance was high for the white and Sylheti women, for whom only
7% and 5% respectively, of women originally enrolled dropped out at
some point during the study. In contrast, non-compliance among
migrants was considerably higher at 20%, with child migrants and
second generation women responsible for most drop outs. The majority
of cancellations occurred before saliva collection had started, while
those women who did start collecting were less likely to quit. This bias
may have been due to British-Bangladeshis having busier and more
complicated lives compared to adult migrants who are mostly at home
and, consequently, perhaps more willing to find time to collect samples.
Conversations with participants support the notion that a change in
attitude towards less commitment among younger generations has also
to do with issues of identity. Second generation women who, were much

more difficult to convince to participate in the study often cited lack of interest as their reason.

Recruitment procedure

Since over 95% of Bangladeshi migrants to the UK originate from Sylhet District in NE Bangladesh (Gardner, 1995b), this was chosen as the target area for recruitment of Bangladeshi sedentees. Sylhet town is the biggest settlement in the area (2,365,200 inhabitants) (http://www.solution.com/SYLHET/) and the origin of a large number of migrants to the UK in past decades. The villages of Barokote and Uttar Royghar in Golapganj Thana, Sylhet District (about 15 km southeast of Sylhet town) were chosen as places from which to recruit participants with a more rural background to match the often rural origin of many UK female migrants. All women were contacted through networking and word of mouth by a team of bilingual research assistants. Recruitment in Bangladesh was undertaken from January to April 2002.

In London, Bangladeshi women were contacted by bilingual (Sylheti-English) workers at local schools, community centres, mosques and sport centres in the boroughs of Tower Hamlets and Camden, where the London population of Bangladeshis is concentrated (ONS, 2001a). A series of workshops on reproductive health were organised with the help of link workers in several community centres, aimed at introducing the team of investigators to the community, and to invite potential volunteers to participate in the study. Almost all white women were recruited through advertisements in local Camden and East London newspapers. The bulk of recruitment in London was completed between May and November, 2002, prior to Ramadan that year. About 20 more women were recruited during May-July, 2003.

The eligibility criteria of the hormonal study restricted recruitment to women of reproductive age, who were not currently (or had not been for at least the past three months) pregnant, lactating, or using steroid-

based contraceptives (oral, injectables, implants or steroid-releasing IUDs). Such criteria imply an inherent bias toward women who are either trying to conceive, women with completed families, or women who are neither but are not steroid-contracepting. The differential impact of the study eligibility restrictions on each of the study groups depended on each group's demographic characteristics and reproductive patterns and resulted in groups with significantly different age profiles (Table 1). In the context of the Bangladeshi community, where pregnancy outside marriage is proscribed and reproductive patterns include high fertility and extended lactation (Thompson, 1982), the recruitment was biased in two ways: towards young single women (especially for the Sylheti women, second generation migrants and, to a lesser extent, among child migrants), and towards older women with completed families (especially marked among adult migrants and white women). In the case of the latter, the high overall prevalence of steroid contraception introduced a bias towards comparatively older women attempting to conceive. For this reason, all relevant analyses where controlled for age.

As part of the study, women completed a general questionnaire requesting information on demographics, socio-economic status (SES), reproductive, migration and health histories, occupation and activities. These data were used to make inter-group comparisons and to evaluate changes in standards of living, reproductive patterns and lifestyle due to the experience of migration. The questionnaire took on average 45 minutes to complete and was administered on a one-to-one basis in either English or Bengali by a bilingual female researcher (see Appendix A). A small proportion (15%) of participants in the white group completed their own questionnaires. Responses were coded and entered in spreadsheet databases for further statistical analysis.

All proportions were rounded up to the nearest unit for reporting results in the text, tables and figures. Percentages may, therefore, not always add up to 100%. The tables also exclude data for respondents for whom

there is missing information. This means that the reported number of cases in particular categories may vary slightly from table to table. All differences mentioned in the text were found to be statistically significant at the 95% confidence level. Where cross tabulations contained less than the required number of cases per cell, statistical analyses were not performed and only descriptive results were discussed in the text. Statistical analyses were performed using SPSS 10.0 for the Macintosh.

A nutritional questionnaire was also devised to obtain information on food habits and on changes in diet upon migration. The goal was to compare both the relative quality of the diet and the food items regularly consumed by women in the different groups. Its primary aim was to inform discussion of the hormonal results and was not intended as a detailed quantitative nutritional intake assessment. The questionnaire was based on a previously validated instrument used with the Bangladeshi community in London (Kassam-Khamis, 1996). A preliminary version was piloted among a group (n=10) of Bangladeshi and white women who attended the same community centres where recruitment for the main study was conducted.

A revised version of the questionnaire was then translated into Bengali and consisted of two parts, the first focusing on dietary habits, and the second consisting of a semi-quantitative food frequency questionnaire (SQFFQ) with a total of 47 closed and multiple-choice questions. Some questions were adapted and tailored to each group to make them pertinent to their cultural context (see Appendix B). The entire questionnaire took an average of 30 minutes to complete and was administered, for the Bangladeshi participants, by a female researcher either in Bengali or English, according to participants' preferences. Except for a small proportion of women (15%) who completed the questionnaires on their own and returned them to the researchers by post, white women also had the questionnaires administered by a female research assistant.

Data from the nutritional questionnaire were entered and coded in a database. The responses were given a score according to the frequency of consumption of particular foods: rarely or never (0), low (1), medium (2), high (3) and very high (4), which corresponded to: rarely or never, less than once a week, once-thrice a week, daily and more than once daily, respectively. Statistical analyses were performed using SPSS v.10.0 for the Macintosh. Kruskall-Wallis Chi-square tests were used to identify trends across all groups. The significance level was set at $p<0.05$.

The research protocols were approved by the East London and the City Health Authority Research Ethics Committee, the Camden and Islington Community Health Services NHS Trust Local Research Ethics Committee, and the joint UCL/UCLH Committee on the Ethics of Human Research. Written informed consent was obtained from all participants in the study. All data were collected and stored in compliance with the Data Protection Act, UK. Participants were identified by a code number in the analyses and their personal details kept confidential.

Table 1. Age distributions of women by group

	SYL	ADU	GROUP CHI	2ndGEN	WHI
Age (yrs) (X ± SE)	26.1 ± 0.6 [a]	31.8 ± 0.7 [b]	27.8 ± 0.6 [c]	24.4 ± 0.6 [d]	31.2 ± 0.7 [e]
n	52	62	50	34	50
range	19-37	21-39	20-38	20-32	22-39
median	25	32	28	25	32

Significance levels for pairwise comparisons are Bonferroni-adjusted.

One-way ANOVA $F_{4,244}$=22.02; $p<0.01$

[a] < ADU, WHI $p<0.01$

[b] > SYL, CHI, 2ndGEN $p<0.01$

[c] < ADU, WHI $p<0.01$; > 2ndGEN $p<0.05$

[d] < ADU, WHI $p<0.01$; <CHI $p<0.05$

[e] > SYL, CHI, 2ndGEN $p<0.01$

CHAPTER 2

BACKGROUND OF THE STUDY POPULATION: HISTORY AND SOCIO-ECONOMIC CHARACTERISTICS OF THE BANGLADESHI COMMUNITY IN THE UK

Introduction

This chapter presents a suite of demographic and socio-economic information collected from first and second generation Bangladeshi immigrant women of reproductive age (19-39 years) living in London that provides a context for the hormonal data presented in Part II and III of this dissertation. For comparative purposes, similar cross-sectional data were also collected from a group of Bangladeshi sedentees in Sylhet, northeastern Bangladesh, and a group of white women living in similar neighbourhoods as the Bangladeshi immigrants in London. Census data provide evidence that socio-economic indicators are highly correlated to geographical area, irrespective of the ethnic background of the groups in question. White households living in the same boroughs as Bangladeshis have indicators more similar to those of their neighbours than to those of the national white population, which makes them a valid reference group for the aims of this study. Attempts to match groups on this basis are supported by close similarities in factors such as housing tenure, educational attainment and employment outlined further below. Following the same rationale, Sylheti women in Bangladesh were recruited from families with kin living in the UK.

Figure 1. Map of Bangladesh

The Bangladeshi community in the UK

History and background

The current population structure of the UK Bengali population in London with all its attendant dynamics cannot be understood without reference to its specific migration history. First migration dates back to the East India Company in the 18th and 19th centuries when the British Merchant Navy employed Bengalis as seamen. These men originated from many areas of East Bengal but, by the 1930's and 40s, as a result of the ship's foremen's preference for hiring kin and fellow villagers, seamen were mostly from Sylhet District (Figure 1). After "jumping ship" some Sylhetis established themselves in ports such as the Docklands area of East London, but also in Cardiff, South Shields and Sunderland, all of which had shipping connections with India and the Far East (Adams, 1987). Here, lodging houses were set up for "lascars" (as these seamen where known, the word originating from a Persian term for "army" or "camp" (http://www.lascars.co.uk/plafeb1931.html).

Relatively few seamen, however, settled in Britain until the 1950s when, in response to the rapid expansion in demand for unskilled industrial labourers, the government launched a voucher system to actively recruit settlers into London, Birmingham, Bradford and Manchester. The seamen's male kin were the first to come, and those who settled in East London worked as labourers in small factories and in the clothing trade. By all accounts, this first generation of immigrants never intended to settle permanently in the UK, but wanted to make their fortunes and return to their country of origin. Men lived for many years alone until the opportunity to go back to Bangladesh no longer seemed plausible. The economic recession of the mid-1960s in the UK with rising unemployment, coupled with a deteriorating economic and political situation in Bangladesh preceding the 1971 civil war, convinced temporary residents that they would never be able to accumulate sufficient wealth to retire in luxury to Bangladesh. It was then that the

mentality changed from sojourner to settler. Many men began to bring over to the UK, first their sons, and later their daughters and wives. This process was often slow due to the costs involved, difficulties associated with immigration applications, lack of suitable lodgings, fear of social harassment, and concern about exposing Bangladeshi women to Western values and influence.

These trends in immigration continued until the early 1970s when, in response to the economic recession, modifications to the existing immigration laws effectively prevented any further entry into the UK of individuals with no prior connections to current residents. The 1971 civil war in Pakistan, which resulted in the eastern part of the country becoming Bangladesh, marked the last major influx of primary immigrants from Bangladesh. Since 1973, only those who have close relatives (elderly parents, spouses and children) already in the UK have been allowed to settle in Britain. Thus, it was during the 1970s and early 1980s that most family reunions occurred. Since the immigration law reforms of the late 1980s, migration of Bangladeshis has continued, but at a much lower rate and under even tighter regulations (Eade et al., 1996a; Summerfield, 1996; Qureshi, 1998).

In 2002, 7.6% (4.5 million) of the total population in the UK were from an ethnic minority. Bangladeshis comprised 0.6% of the total UK population, and 6.1% of minority ethnic groups. Four out of 5 Bangladeshis in the UK live in large urban areas, and 54% live in London where they represent 3.8% of its population. Of the 154,000 Bangladeshis living in London, the boroughs of Tower Hamlets and Camden have the highest concentrations at 43% and 8%, respectively. The presence of Bangladeshis in these areas represents roughly 40% and 6% of the total borough population respectively (ONS, 2001a, 2002). Most participants in this study have lived in London since arrival in the UK, although a small proportion (12%) lived outside London before moving to the capital.

For the sample under discussion here, the purpose of migration for first generation female migrants (overseas-born Bangladeshis) depends largely on the age at which immigration occurred but generally reflects the history outlined above. (Table 2 shows the median age on arrival and the median length of time in the UK for first generation migrant groups). The majority of women who arrived in the UK as adult migrants came as brides or to join their husbands who were already settled in the UK. Women who migrated as children or as adolescents typically arrived as primary migrants along with their families, or came to join their long-term resident fathers in the UK. The timing of arrival of women's parents into the UK also mirrors the already known history of Bangladeshi immigration, although it appears that earlier migrants often brought their wives and families relatively soon after their arrival compared with later migrants who did not reunite with their families until over two decades later, reflecting the immigration law reforms of the 1980s (Table 3).

In general, the Sylhetis who emigrated to Britain were mostly Sunni Muslims. They were not drawn from the poorest sections of the population, but came from middle-income groups who could afford the cost of a sea passage. They were mainly village folk from small land-owning families from particular areas of Sylhet District such as Mulvi Bazaar, Biswanath and Beani Bazaar as well as from Sylhet town (see Figure 1). In some villages in these *thanas* (administrative districts), every household currently has a family member in Britain (Gardner, 1995b). This explains why the Bangladeshi population tends to be reasonably homogeneous both culturally and socio-economically compared with other South Asian groups in Britain (Carey & Shukor, 1985).

Table 2. Age on arrival and length of time in the UK of first generation Bangladeshi migrants

| | GROUP | |
	ADU	CHI
Age on arrival in the UK (yrs) (X ± SE)	19.6 ± 0.5	7.5 ± 0.5
n	62	50
range	11-34	0.75-14
median	20	8
Length of time in the UK (yrs) (X ± SE)	13.1 ± 0.8	21.2 ± 0.6
n	62	49
range	1-24	12-32
median	14	22

Table 3. Migration history of first and second generation Bangladeshi groups in the UK

| | | GROUP | |
	ADU	CHI	2ndGEN
Purpose of migration (% within groups)			
marriage	49	..	..
join husband	13	..	..
accompany family	23	4	..
join father	15	96	..
Migrated with: (% within groups)			
husband	56	..	..
parents & siblings	17	6	..
mother & siblings	19	94	..
children	8	..	..
Domicile in Bangladesh before migration (% within groups)			
Village	72	62	48
Sylhet town	17	36	52
Dhaka City	12	3	..
Occupation on arrival in the UK (% within groups)			
housewife	61	2	..
job/ volunteer	13	..	..
student	26	68	..
child	..	30	..
Father's year of arrival in the UK (% within groups)	*(n=10)*	*(n=25)*	*(n=29)*
1930s	10	..	..
1950s	30	24	14
1960s	50	52	59
1970s	..	24	28
1980s	10	..	..
Mother's year of arrival in the UK (% within groups)	*(n=13)*	*(n=35)*	*(n=31)*
1960s	8	..	26
1970s	15	37	58
1980s	69	57	16
1990s	8	6	..
Difference between mother's and father's year of arrival in the UK (yrs) (% within groups)	*(n=9)*	*(n=24)*	*(n=29)*
0-10	11	16	63
11-20	55	49	31
21-30	33	32	3

Sample sizes are SYL (52), ADU (62), CHI (51), 2ndGEN (34), WHI (50) unless otherwise stated.

The place of origin of Bangladeshi migrants in this study appears to have changed with time. Early arrivals (constituting second generation, British-born Bangladeshis) are as likely to be from Sylhet town as from a village in Sylhet District, whereas more recent migrants are more likely to be from a rural background, with a few migrants from the capital city of Dhaka. This trend may reflect changes in both living standards as well as expectations of the residents of Sylhet town over the past decades. Originally, migrants were small landowners for whom overseas migration seemed a profitable venture. Over the years, remittances from the UK have created a more affluent class in Sylhet town; they are perhaps more inclined to stay in Bangladesh and establish businesses than their rural counterparts. As a consequence, since primary migration into the UK is almost non-existent, any newcomers are mostly spouses or close kin of people already settled in the UK. This has promoted immigration primarily from the rural villages from where many such families originate.

Demographics

Bangladeshis are the fastest growing ethnic minority in the UK, with an annual increase rate of 30% over the past decade. Overseas-born Bangladeshis have fertility rates three times the UK national average, and almost twice as high as any other ethnic group (Scott et al., 2001). They show extremely high fertility at younger ages, but also a significantly higher rate of childbearing at older ages compared to other groups. This is, in part, a result of a resumption of childbearing first started overseas which then continued when women reunited with their husbands on migration to the UK (Diamond & Clarke, 1989).

Bangladeshis, like most minority ethnic groups, also tend to have a younger age structure than the white population. Forty percent of all Bangladeshi immigrants in the UK are under 14, which is double the proportion of whites, while less than one-third (6%) are over 65 compared to 21% for the white population. The median age for

Bangladeshis is 18 years compared to 37 for whites (Summerfield & Babb, 2003). These statistics are even higher for Bangladeshis who were born in the UK: over two thirds are aged 0-14, and only 6% are over 30 years old (Scott *et al.*, 2001).

A distinctive feature of the Bangladeshi population is its age/gender pyramid, which is the most irregular of all ethnic groups. There is a heavy male bias among overseas-born Bangladeshis, with an overall ratio of 100:64 males to females. In comparison, the ratio for British-born Bangladeshis is more or less symmetrical (Eade *et al.*, 1996a; Summerfield & Babb, 2003). This unequal pattern is explained by the particular history of migration to Britain described above, where men lived alone for many years before being joined by their wives and children in the 70s and 80s (Qureshi, 1998).

Marital status

The high fertility evident among the Bangladeshi population is partly due to the almost universal pattern of early marriage and the norm of large family sizes (Haskely, 1996). However, data from this study indicates that this trend is changing. Although the average age at first marriage was similar for all migrant groups in the sample (no data for white women), a closer examination of the number of single women per birth cohort in each of the three migrant categories revealed a trend towards delayed marriage in younger generations, in particular in the British-born group (Table 4). For instance, 93% of adult migrants born in the 70's are currently married compared to 79% of child migrants and 52% of second generation women. The differences among those born in the 80's are even more pronounced: the proportions of currently married women are 67%, 14% and 15% for adult migrants, child migrants and second generation, respectively. Interestingly, an aspect that does not seem to have changed between contemporary Bangladeshi migrants is the median age difference between women and their spouses (5 vs. 6 yr for

first and second generation, respectively). However, such age difference was only half of that found in the Sylhet group (median 11 yr), and of that among the generation of their parents.

For the Sylheti group, the observed median age at first marriage (19 yr) is only slightly older than that reported for Sylhet district (18.4 yr) (NIPORT, 2001). However, the birth cohort analysis revealed a sizeable number of women in the Sylheti group well past this median age at marriage. It is likely that the length of time now spent in full-time education by this cohort could account for the delay (see section on education), but it could also be related to the fact that many of these women happened to be the last siblings in the family. According to Sylheti customs, a female cannot marry until her older sister(s) have a spouse, a tradition that may considerably delay the marriage of younger siblings in a large family. It is unclear to what extent this custom has relaxed among Sylhetis in the UK.

In the white group, the large number of single women in the older age range may reflect cultural attitudes towards marriage. For instance, the white women in the present sample are equally likely to cohabit with non-marital partners as they are to be married. In contrast, there is as yet relatively little manifestation of Western patterns of non-marital cohabitation among British-Bangladeshis (Berrington, 1996; Eade *et al.*, 1996a).

Table 4. Marital status by group

	SYL	ADU	GROUP CHI	2ndGEN	WHI
Marital status (% within groups)					
single	69	5	28	62	60
married	29	82	66	36	16
separated	2	8	2	..	2
divorced	..	2	4	3	4
cohabiting	..	..	..	..	16
widow	..	3	..	..	2
Marital status by birth cohort (% within cohort by group)					
1960-1969	(n=7)	(n=29)	(n=4)	(n=0)	(n=23)
single	29	..	..	..	39
ever married	71	100	100	..	61
1970-1979	(n=39)	(n=30)	(n=39)	(n=21)	(n=26)
single	77	7	20	48	77
ever married	23	93	79	52	23
≥1980	(n=8)	(n=3)	(n=7)	(n=13)	(n=1)
single	75	33	86	85	100
ever married	25	67	14	15	..
Age at first marriage[a] (X ± SE)	20.1 ± 0.8	19.1 ± 0.3	20.0 ± 0.4	20.0 ± 0.9	..
n	15	57	36	14	..
range	16-26	13-24	16-26	16-25	..
median	19	19	19.5	19	..
Age at first marriage[b] (X ± SE)	28.8 ± 0.9	19.6 ± 0.4	22.0 ± 0.7	23.8 ± 0.7	..
n	53	60	50	34	..
events	15	57	36	14	..
censored	38	3	14	20	..
Age differences (yrs) between women and their husbands/partners [c] (X ± SE)	11.2 ± 2	5.2 ± 0.4	5.3 ± 0.8	6.6 ± 1	0.8 ± 0.9
n	10	46	28	11	12
range	5-22	1-13	-1-17	0-14	-4-7
median	11	5	5	6	1
Age differences (yrs) between women's father and mother[d] (X ± SE)	12.4 ± 1	16.3 ± 5.5	12.1 ± 2.0	6.9 ± 1.2	..
n	25	3	9	16	..
range	5-25	7-26	5-20	0-20	..
median	12	16	14	6.5	..

Sample sizes are SYL (54), ADU (62), CHI (51), 2ndGEN (34), WHI (50) unless otherwise stated.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] Closed cases only: One-way ANOVA $F_{3,121}$=1.2 p>0.05

[b] Kaplan-Meier survival function; MIGRANT GROUPS only: Logrank 73.13, df=3, p<0.001

[c] One-way ANOVA $F_{4,102}$=10.59 p<0.01; SYL > ADU, CHI, WHI p<0.05; WHI < all groups p<0.01

[d] One-way ANOVA $F_{3,49}$=4.5 p<0.05; SYL, ADU >2ndGEN p<0.05

Socioeconomic characteristics

Household size and composition

The demographic structure, cultural traditions and economic characteristics of the Bangladeshi community in the UK underlie its distinctive patterns of family formation, household size and composition. Bangladeshi households in the UK are on average twice as large as those of the white population, reflecting their higher fertility, and three times as large as the average household in London (ONS, 2001a, 2002). Half of all Bangladeshi households are comprised of 5 people or more, and only a fourth number less than 3 people. This is in sharp contrast with figures for the total UK population (7% for households >5 people, and 64% for households <3) (DWP, 1999; Summerfield & Babb, 2003). Almost half of all Bangladeshi families have 4 or more children compared to only 4% of white families, most of whom have 1 or 2 children (ONS, 2001a). In addition, among Bangladeshi families there is often a large age difference between siblings, with older children being born in Bangladesh before migration, and younger ones born in the UK after husbands and wives reunited (Qureshi, 1998).

Households are not only large but also multi-generational. It is not uncommon to have three generations in one household, with grandparents living with their married children and grandchildren (Eade *et al.*, 1996a). This situation occurs in only 1% of white households (ONS, 2001a). In contrast, single parent households -- mostly single mothers -- are half as common among Bangladeshis (12%) than among whites (26%), and where they do occur, women are either widowed, divorced or separated rather than unmarried. Over two-thirds (87%) of Bangladeshi children aged 0-14 live with both natural parents, compared to 73% of white children (Penn & Lambert, 2002). Bangladeshi households thus show a traditional pattern of extended family households.

In the sample reported here, except for one second generation woman, all Bangladeshi women live in their family home, either as daughters, mothers or wives (Table 5). In contrast, white women are more likely to live on their own, or with just their partners, with other unrelated adults or as single parents. Mirroring UK national statistics for household size (DWP, 1999; Summerfield & Babb, 2003), 52% of white women live in single-person or two-people households, compared to only one-ninth of child migrants and second generation women and even fewer adult migrants (3%) and Sylheti women (6%). Instead, over half the women in all four Bangladeshi groups live in households with 5 people or more, compared to less than 10% of the white women.

Significantly larger households (average 5.1 people) were found in this study among Bangladeshi migrant groups than in the white group (2.6 people); this is in line with current statistics for the UK, which show an average household size of 4.7 for Bangladeshis and 2.3 for whites (ONS, 2001a, 2002). The contrast between the Bangladeshi households and the general population in London is even greater considering that the average household size in London is 1.6 (ONS, 2001a), less than half the statistic calculated for the migrant groups in our sample.

While Sylheti women in Bangladesh are more likely to live in extended families with their husband's parents and/or siblings–in law, the custom of virilocal residence is becoming less common among Bangladeshi families in London. This may possibly reflect space constraints in the type of accommodation available, but may also reflect the acquisition of Western ideals about private space for the nuclear family. Since second generation Bangladeshis are only now reaching reproductive age, it remains to be seen whether mirroring the change in family structure, there will also be a decline in average family size among these British-born Bangladeshis.

Table 5. Household characteristics by group

	SYL	ADU	GROUP CHI	2ndGEN	WHI
Type of houshold (% within groups)					
partner only	..	..	10	3	28
nuclear family (partner and children or parents and siblings)	63	75	67	82	22
extended family (in laws, aunts, uncles, cousins, grandparents)	33	18	20	9	2
children only	4	7	2	3	16
self	..	..	..	..	16
non kin (housemates, friends, lodgers)	..	..	..	3	16
Household size (% within groups)					
1 person	..	..	..	3	16
2 people	6	3	12	9	36
3 people	..	13	10	15	32
4 people	11	22	19	12	8
5 people	13	32	25	21	6
6+ people	69	30	33	41	2
No. people in the household [a] (X ± SE)	6.9 ± 0.4	5.0± 0.2	5.0 ± 0.3	5.2 ± 0.4	2.6 ± 0.2
range	2-15	2-9	2-10	1-12	1-6
No. of children aged 16 or under [b] (X ± SE)	2.1 ± 0.2	2.5± 0.1	2.5 ± 0.2	2.3 ± 0.3	1.8 ± 0.2
range	1-5	1-5	1-6	1-5	1-4

Sample sizes are SYL (54). ADU (62). CHI (51). 2ndGEN (34). WHI (50) unless otherwise stated.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] One-way ANOVA $F_{4,26}$=27.2 p<0.01; SYL >all groups, WHI< all groups p<0.01

[b] One-way ANOVA $F_{4,19}$=1.8 p>0.05

Housing characteristics

In terms of housing tenure, Bangladeshis in the UK have a high dependence on council housing. About half live in dwellings rented from a local authority compared to only a third who live in owner-occupied accommodation. About one fifth of Bangladeshi homes are overcrowded (with over 1.5 persons per room) (ONS, 2002). In the sample reported here (Table 6), the second generation women tend to live in larger accommodations than their first generation counterparts (5.2 vs. 4.6 rooms/household), for whom the number of rooms available for the family is smaller than the national average of 5.2 (ONS, 2001a). This difference may reflect the higher proportion of house- (53%) as opposed to flat-residents (38%) in the second generation group. Most early migrants settled in East London, where larger council houses were available. For later arrivals, who tended to settle in Camden, government housing is mostly comprised of flats. One of the biggest drawbacks to life in London frequently mentioned by migrant Bangladeshis is the compromise in living space. In contrast, dwellings for the Middle Class in Bangladesh are significantly larger (6.2 rooms). Here, the most common type of village residence is still a rambling chalet-type house, often situated within a group of such houses to accommodate other relatives. With the economic boom brought about by remittances from overseas, however, new housing is being built following Western ideals, and flats have become fashionable among families receiving remittances from abroad. This is particularly true for towns like Sylhet where many affluent people rent, rather than buy, such accommodation.

Household density figures for all three migrant groups (2.3, 2.0 and 1.7 persons/room for adult, child and second generation groups, respectively) indicate that women in our sample live in overcrowded homes where bedrooms often house over 4 people and living rooms are converted into additional bedrooms at night. Given current economic constraints, the overcrowding of Bangladeshi households in London, especially Camden, is unlikely to improve in the near future. Such over-

crowding is partly maintained by the conservatism of Bangladeshi communities and their considerable social and economic disadvantages that translate into limited opportunities for geographical mobility. Traditionally, Bangladeshis have remained geographically confined in well-established areas that cater for their religious and cultural needs (Eade *et al.*, 1996a). Observations in the field suggest that, even though newly married couples move out from their parent's households, they tend to remain in the same neighbourhood as their close family.

However, this pattern is also slowly changing. Some families with higher education are often relatively better off (data not shown) and are therefore better able to break the reliance on social housing. These more affluent households can move to other neighbourhoods, have fewer household members, occupy larger dwellings, and presumably enjoy a better quality of life. Owner-occupiers are more likely to be second generation Bangladeshis (56%) and, to a lesser extent, child migrant households (29%). The families of these women have been in the UK for longer and, presumably, have capitalised on opportunities for acquiring property. This is reflected in the fact that home ownership is more common in East London where initial migration occurred than in Camden. Nonetheless, owners tend to buy and occupy ex-council accommodation probably because the prices of these homes are below market value. More recent arrivals (adult and child migrants) mainly live in rented local authority accommodation. In contrast, British-born Bangladeshis in rented accommodation are more likely to have a private landlord, reflecting their better economic position. Home ownership and private letting among the second generation group reported here is considerably higher than the 33% and 10%, respectively, reported in the 2001 Census for the Bangladeshi community nationwide (ONS, 2001a). It is possible that this phenomenon is a London peculiarity, and not necessarily a generalisation applying to all second generation Bangladeshis in other parts of the UK.

In contrast with the reported UK national average for the white population (71% ownership and 20% letting from the social sector (ONS, 2001a)), white women are more likely to rent (60%) than to own (40%) a home, with half the sample living in dwellings rented from their local authority. Although these proportions suggest that the white women in the study are on average of low socio-economic background, there are, despite efforts to ensure marching, still differences at least in terms of housing tenure and other accommodation characteristics between white and Bangladeshi groups in this study.

Table 6. Accommodation characteristics by group

	SYL	ADU	GROUP CHI	2ndGEN	WHI
Type of accommodation (% within groups)					
flat	38	72	57	38	56
house	61	11	22	53	30
maisonnette	..	15	20	9	14
hostel	..	2	..	..	..
Accommodation tenureship (% within groups)					
rent	19	87	71	44	60
own	81	13	29	56	40
Accommodation rented from (% within groups)					
council/ housing association	..	96	94	62	48
private	..	4	6	38	52
Address in London (% within groups)					
East London	..	39	67	67	..
Camden /Kentishtown	..	55	29	17	..
Other (greater London)	..	6	4	17	..
No. rooms for use of the family * ^{a}(X ± SE)	6.2 ± 0.2	4.5± 0.1	4.6± 0.1	5.2± 0.2	4.5± 0.2
range	3-11	2-7	3-7	2-7	1-7
Density (No. people per bedroom) ^{b} (X ± SE)	1.8 ± 0.1	2.3 ± 0.1	2.0 ± 0.1	1.7 ± 0.1	1.1 ± 0.1
range	1-7	1-6	0.5-4.5	0.5-3	0.5-2

* includes living rooms, bedrooms, kitchen, utility rooms but NOT bathrooms nor storage rooms.

Sample sizes are SYL (54), ADU (62), CHI (51), 2ndGEN (34), WHI (50) unless otherwise stated.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

^{a} One-way ANOVA $F_{4,237}$=17.69 p<0.01; SYL >all groups p<0.01; ADU< 2ndGEN p<0.05

^{b} One-way ANOVA $F_{4,235}$=14.35 p<0.01; WHI <all groups p<0.01; ADU> SYL p<0.01; ADU> 2ndGEN p<0.01

Education

Most immigrant Bangladeshis have only an elementary education obtained in their country of birth, and a large proportion have no educational qualification at all. Scholastic achievement of Bangladeshi children is at a level below the UK national average, and is lower than that of many other ethnic minority groups (Ghuman, 2002; ONS, 2002). However, most young Bangladeshi boys and girls also attend both religious education classes and/or Bengali language classes outside of normal school hours (Brooker, 2003a).

These general findings are matched by information obtained from the sample under consideration here (Table 7). Women who arrived in the UK as adults have significantly fewer years of education (on average 4.5 years less) than all other groups in the study. However, there are no differences between child migrants, second generation women and white women in educational attainment. The lower educational achievement of adult migrants (9.6 yr) compared to their counterparts in Sylhet (12.8 yr) itself may be accounted for by the high proportion of adult migrant women from a rural background where educational opportunities are more limited. There is no equivalent disparity among child migrants who are also predominantly of rural origin. Child migrants, on average, continued their education in the British system following their arrival in the UK. However, an analysis of the effect of age at migration on years of education shows that women arriving during puberty were less likely to pursue further schooling. Instead, following Sylheti tradition, they remained at home in preparation for an early marriage. Since most adult migrants arrived as brides, or already had a family, age at arrival had no effect on educational attainment. For these adult women, the opportunity to go into formal education was correspondingly small. However, many women in this group have since been involved in skill development courses at local community centres. The effect of marriage on years of education was significant for all groups in the study, with single women having on average 3.6 more years of education than their ever-married

counterparts. Among those ever-married, age at first marriage had a negative impact on educational attainment, especially among Sylheti and adult migrant women; younger brides had up to six less years of schooling than older ones.

Table 7. Education by group

	SYL	ADU	GROUP CHI	2ndGEN
Participant's education (yrs) [a] (X ± SE)	12.8 ± 0.5	9.6 ± 0.5	12.9 ± 0.4	14.0 ± 0.4
n	52	60	49	34
Partner's education (yrs) (X ± SE)				
UK-educated [b]	..	13.1 ± 0.6	15.6 ± 1.3	16.5 ± 3.7
	..	13	6	2
Bangladesh-educated	11.9 ± 0.7	10.5 ± 0.5	11.1 ± 0.6	12.2 ± 1.0
	16	38	26	9
Father's education (yrs) [c] (X ± SE)	11.6 ± 0.4	8.4 ± 0.7	7.9 ± 0.8	7.9 ± 1.0
n	52	53	39	24
Mother's education (yrs) [d] (X ± SE)	7.4 ± 0.5	5.2 ± 0.6	4.8 ± 0.6	5.7 ± 0.9
n	51	58	47	32
Education (yrs) by marital status [e] (X ± SE)				
single	13.9 ± 0.5	14.3 ± 1.15	14.6 ± 0.6	15.0 ± 0.4
	36	3	13	21
ever married	10.2 ± 1.1	9.3 ± 0.5	12.2 ± 0.5	12.5 ± 0.5
	16	57	36	13
Education (yrs) by rural/urban background (SYL group only) [f] (X ± SE)				
village	9.0 ± 2.0	..	..	..
	7			
town	13.4 ± 0.5	..	..	..
	45			

Sample sizes are SYL (54), ADU (62), CHI (51), 2ndGEN (34), WHI (50) unless otherwise stated.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] One-way ANOVA $F_{4,240}$=19.15 p<0.01; ADU <all groups p<0.01

[b] One-way ANOVA $F_{4,133}$=2.39 p>0.05

[c] One-way ANOVA $F_{4,210}$=5.61 p<0.01; SYL> ADU, CHI, 2ndGEN p<0.05; WHI> CHI p<0.05

[d] One-way ANOVA $F_{4,230}$=11.48 p<0.01; WHI> all groups p<0.01

[e] Two-way ANOVA $F_{2,235}$=14.04 p<0.01; group p<0.01; marital status p<0.01; interaction ns.

[f] T-test t=-2.94, df=50 p<0.01

Correlation education (yrs) vs. age at marriage r= 0.37, p<0.01

Partner's education

There were no significant differences between groups regarding their partners' average years of education, and all groups display a similarly wide range (0-20 years) (Table 7). Partners of migrant women who were educated in Bangladesh and, therefore, presumably arrived as adults for marriage, have fewer years of schooling (on average 3 yr less) than partners of women born and/or raised in the UK. Thus, it turns out that child migrants or second generation women married to partners educated in Bangladesh have higher educational achievements (on average 2 years more) than their husbands, while women married to men educated in the UK tend to have fewer years of schooling (on average 3.5 years less). For the Sylheti group, the difference in educational levels always favours the man, and is even more accentuated in village couples, where men have on average 4 years more schooling than women, compared to the average difference of one year between Sylhet town couples.

Such educational disparities suggest that traditional expectations regarding the socio-economic and educational status of a potential partner have relaxed among Bangladeshi migrants in the UK. Many parents who are resident in the UK still regard potential spouses brought up in Bangladesh as "good matches" for their children. In arranging these marriages, parents are seemingly willing to overlook differences in social standing that would normally be non-negotiable in exchange for a conservative and religious-minded suitor from the home country. For the overseas groom, the possibility of legal migration into the UK through marriage is probably sufficient incentive to overlook traditional codes of social mobility (Summerfield, 1996). In other words, immigration regulations and cultural perceptions about what constitutes a good partner have created ideal conditions for what are in reality very unequal marriages on other levels. These inequalities have potential repercussions for later family dynamics and individual well-being. This

situation is likely to change in the future as British-born generations distance themselves from traditional marriage patterns.

Parents' education

There were no significant differences between migrant groups regarding the educational levels of participant's fathers or mothers. Fathers of women still living in Sylhet were more highly educated than fathers in all migrant groups to London (average difference of 4 years of schooling) (Table 7). This may be explained by the presence of a larger number of fathers of rural origin among the migrants than in the Sylheti group. The fact that there are no significant differences in paternal education between white women and their migrant counterparts again validates the matching of groups by location and socioeconomic status. In contrast, despite the large heterogeneity in all groups, mothers of women in Sylhet and in the migrant groups were matched in terms of their educational attainment, but were significantly less educated (on average 4.5 years less schooling) than mothers of white women. Furthermore, the differences between father's and mother's years of education among Bangladeshi couples are statistically significant, while such a difference is not evident for white parental couples.

Employment

Following the crisis in factory employment in Britain during the 1970s, the occupational pattern of migrant Bangladeshis shifted to the catering industry. The origin of this shift was the monopoly Bangladeshis had as cooks and galley hands aboard British ships in the early days of migration. Once on shore, they continued this speciality in tea houses and cafes opened on the waterfront, and these expanded in number to meet the demands of single men living and working in London's Docklands area (Adams, 1987). The 20 restaurants or small cafes owned by Sylhetis in 1946 grew to more than 3,000 by 1980. In 2002,

approximately 90% of the "Indian restaurants" in the UK were actually owned by people of Sylheti origin (Gillan, 2002). Rates of self-employment among British-Bangladeshis are therefore marginally above the UK national average (Berthoud, 1998; ONS, 2001a).

Despite the expansion of the catering industry, Bangladeshi men and women have, respectively, four to six times higher rates of unemployment compared to the white UK population. These rates are the highest of all ethnic minorities. In addition, while two-thirds of Bangladeshi men aged 16 and over are employed in the catering industry, they mostly hold menial jobs. Only a sixth of Bangladeshis – less than half the UK national average, and lowest of all ethnic groups -- are employed in professional and managerial roles. Bangladeshi women have little participation in the formal labour market; only a fifth of women aged 16 or over has ever worked. The majority of employed women are active in clerical and secretarial jobs, followed by craft, personal service and skilled manual occupations including manufacturing work (Peach, 1996; ONS, 2002). Given this employment pattern, Bangladeshi households are heavily reliant on social security benefits, with reliance rates three times higher than those of the white population. Bangladeshis are much more likely (80%) than other ethnic groups to be living below the fiftieth percentile of the UK national average income, a profile worse than that of white lone parents and white people in post-retirement age (ONS, 2002).

Participant's occupation

In the adult migrant group, the largest proportion of women (69%) classified themselves as housewives, 27% were employed and a small number were students or volunteers. In contrast, the majority of women in the child migrant and second generation groups were employed (58% and 60%, respectively), and in the latter a fifth of the participants were students (18%) (Table 8). The trend towards higher female employment

across generations seemed to be accompanied by a change in the type of jobs performed. Among those employed, 57% of child migrants and 70% of second generation women had non-manual occupations compared to only 44% in the adult group. These changes are likely to be the result of higher educational attainment, better language skills and better cultural integration among British-educated younger generations, as well as changing perceptions regarding women's roles. Interestingly, such changes have the potential to modify family financial relations radically. In the present study, 19% of child migrants and 26% of second generation women were found to be the sole breadwinners in their families. The employment rate reported here for the second generation women (60%) is considerably higher than that reported previously for Bangladeshi women in the UK (13-35%) (Eade *et al.*, 1996a). However, based on our results, it can be argued that this discrepancy may be accounted for by the lack of distinction between first and second generation women in the 1996 survey.

The occupational profile of the white group was fairly similar to that of the second generation migrants in that the majority of women were employed and to a lesser extent were students. Although the overall rate of employment was similar in the two British-born groups (68% vs. 60% respectively), there were still differences in the type of jobs performed; the proportion of white women in manual jobs was half that of their Bangladeshi counterparts (15% vs. 30%, respectively).

With regards to the Sylheti sample, it was comprised of equal number of housewives, students and employees. The effect of marital status on the type of occupation was evident in the fact that no married women classified themselves as a student, and that over half (64%) of the women in employment were single. The relatively high economic participation of this sample is definitely not the norm in Sylhet, but more a reflection of our sample being comprised of middle-class women,

among whom the teaching and administrative jobs reported here are well accepted female occupations.

Partner's occupation

As mentioned earlier, the Sylheti economy relies heavily on commerce and as a result of the wealth created by remittances, many households' source of income is either through commerce or property letting; hence the high proportion (62%) of businessmen among the spouses of women in the Sylheti group (Table 8). The remainder of the sample hold more traditional jobs, such as teachers or civil servants.

In the UK, in contrast to the trend among younger generation women towards non-manual jobs, over half the spouses in all three migrant groups perform manual jobs, most commonly as factory workers in older groups, or waiters and cooks in younger ones.

Reflecting the emerging dominance of younger women in household support and finance, child migrants and second generation women often occupy higher occupations than their partners. In many cases, this reflects a differential educational history if, for example, women were educated in Britain and their partners in Bangladesh. The latter may often lack appropriate language skills and/or educational achievements to obtain comparable jobs to their spouses, and will instead perform manual activities in the catering industry. These differences are less likely to occur in couples where both members were born and/or raised in Britain. Among white women, differences between partners more often favour the male but still tend to be small and, in some cases, non-existent.

Parents' occupation

The fathers of Sylheti women tend to have occupations that are similar to their sons-in-law. Nonetheless, in the older generation there are a higher proportion of farmers and army officers. In the rural areas impacted by remittances, male occupation has shifted in the last decades away from farm-related activities (Table 8). Men in these places are nowadays more likely to be involved in small-scale businesses or to be working abroad as economic migrants. In our sample this is reflected in the fact that although some Sylheti women have a father who is a farmer, none of them have a partner in this occupation.

Among migrant groups in the UK, the type of occupation held by participants' fathers depends on the country where the fathers live. Those men in Bangladesh are civil servants, army officials, work in commerce or as farmers. In contrast, fathers residing in the UK (mostly those of child migrants and second generation women) are employed primarily in manual jobs. The earlier arrivals are often now retired but worked in the textile industry as machinists, or as porters and watchmen for rail companies, while the more recent arrivals are employed in the restaurant industry. The closure of sweatshops and other factories in the East End and the boom of the restaurant sector are mainly responsible for this shift in employment patterns (Carey & Shukor, 1985). In the white group, all of the participant's fathers are employed, and two fifths of them perform manual jobs such as drivers, carpenters and painters.

Employment among the participants' mothers in all Bangladeshi migrant groups is very low, and over two thirds of them are housewives. Those who are employed have either clerical positions or home based jobs such as childminding and piecework sewing, depending on language skills and, indirectly, the time they have been in the UK. In the Sylheti group, the majority of the participant's mothers are also housewives and those in employment (12%) are mostly teachers. In contrast, over two-

thirds of mothers of white women are employed, divided almost equally between manual and non-manual occupations.

Table 8. Occupation by group

			GROUP		
	SYL	ADU	CHI	2ndGEN	WHI
Participant's occupation (% within group)					
housewife	36	69	37	21	8
student	33	2	4	18	16
volunteer	..	3	..	3	2
unemployed	..	..	..	..	6
employed	31	27	58	60	68
Participant's job type (% of all employed)					
non-manual	100	44	57	70	85
manual	..	55	43	30	15
Proportion of participants aged >25 yrs in employment					
	(n=26)	(n=54)	(n=33)	(n=12)	(n=42)
	38	24	51	83	69
Participants as breadwinners*					
% of women employed in their group	19	19	32	45	9
% total women in their group	6	5	19	26	6
Partner's occupation (% within group)					
student	..	..	3	8	7
self-employed	62	..	..	..	..
unemployed	..	8	10	..	4
employed	36	92	86	90	88
Partner's job type (% of all employed)					
non-manual	50	36	48	37	67
manual	50	64	52	63	33
Father's occupation (% within group)					
retired	4	2	2	6	..
self-employed	49	41	2	..	..
unemployed	..	5	4	6	..
employed	47	51	90	88	100
Father's job type (% of all employed)					
non-manual	73	41	25	24	62
manual	27	58	74	76	38
Mother's occupation (% within group)					
housewife	86	95	83	82	6
retired	2	2	..	3	..
unemployed	..	..	..	..	6
employed	12	4	16	15	88
Mother's job type (% of all employed)					
non-manual	100	50	25	60	57
manual	..	50	75	40	43

* criteria: women who are the only ones employed in their household.

Sample sizes are SYL (54), ADU (62), CHI (51), 2ndGEN (34), WHI (50) unless otherwise stated.

Assets in Bangladesh

Over half the women in all migrant groups reported still owning family property in Bangladesh (74%, 65% and 77% for adult migrants, child migrants and second generation, respectively). This is commonly a "*bari*" or ancestral home, namely the house where the family has lived for generations, often with agricultural plots attached. The houses are either now inhabited by relatives or are often empty while rice croppers cultivate the associated land. In addition, encouraged by very cheap building costs, migrants have invested in construction projects in Sylhet that are then rented out as flats or shops. In most cases, the profits do not translate into a significant income in England, but are used to provide for relatives still living in Sylhet. About a fourth (24%) of family businesses in the Sylheti group had been established using such remittances from relatives abroad.

Over a third (38%) of women in the Sylheti group reported that their families received remittances from abroad, most commonly every 3 months. Among village dwellers, this figure was 100%. In Sylhet town, source countries for these remittances were the UK, USA, Canada and, in one instance, Belgium. Remittances from the Middle East were more common among women living in villages. This pattern reflects the change in migrant destinations over the past few decades. When UK regulations made migration to Britain more difficult, men of lower economic status from the rural areas opted to migrate to Arab countries in the Middle East, where the economic boom created a large demand for cheap, unskilled labour (Gardner, 1995b). With increasingly tight immigration laws to the UK and the USA, Middle East destinations could become even more popular among potential migrants, who also benefit from immersion into primarily Muslim cultures rather than secular ones.

For Sylhet District itself, migration has had far-reaching consequences. The local social and economic structures have become globalised. In Bangladesh, regular remittances sent from abroad have meant that

many families who were previously only very small owner-occupiers or sharecroppers have become wealthy landowners. Remittances have generated an expansion in house building, higher disposable incomes, and a cash and boom consumerism. However, this apparent growth of the local Sylheti economy is bound to be finite and temporary. As British-Bangladeshis settle permanently in the UK and tend to have no remaining immediate family connections in Sylhet, wages are and will be invested instead in British businesses and properties. Sylheti businesses that depend on foreign income are guaranteed to suffer, with disastrous repercussions for the local economy (Gardner, 1995b, a). One report has already indicated that, in the mid-90s, only 20% of Bangladeshi families in East London were sending remittances to Sylhet, whereas 85% of Bangladeshi families did so in the 60s and 70s. (Gillan, 2002).

Assets in the UK

The proportion of Bangladeshi women in London whose families own a business is similar for all migrant groups (10% and 15% for first and second generation groups, respectively) as well as for white women (10%), but is significantly smaller than for the families of Sylheti sedentees (69%). The high proportion of business ownership in Sylhet is partly a response to the formal job market, which is limited to the civil service, as well as a reflection of the fact that the local economy has always been commerce-driven. Among migrants in London, family businesses established in the UK almost entirely relate to the catering industry. Some are well-established Indian restaurants and others are more recent investments in Indian take-away outlets. Among white women, businesses are more diverse, ranging from dress making to wedding photography.

Car ownership among Sylheti families (21%) is considerably lower than for migrant Bangladeshi groups in the UK. Among the latter, over half of the households own a car and there is a trend for higher ownership

among longer established groups (54%, 65% and 82% for adult migrants, child migrants and second generation groups, respectively). This trend could reflect the better economic position of child migrants and second generation women, which would allow ownership and maintenance of a car, as well as a more thorough integration and understanding of the host system compared to adult migrants. Car ownership among white women (36%) corresponds to the latest figures for London at 38% (ONS, 2001a, b). Field observations support the notion that the significantly higher proportion of car ownership among Bangladeshi migrants in London may partly result from the need to transport very large families, as well as to facilitate the buying of food in bulk from specialised shops that are often not within walking distance from home.

Acculturation

As already outlined, the Bangladeshi community remains fairly traditional in its outlook and customs, with comparatively little integration with other cultural groups. For example, mixed marriages between Bangladeshis and other ethnic groups in the UK are uncommon. It is estimated that only 4% of Bangladeshi men aged 24 or under are married to a white partner, and this figure is even lower (1.6%) for men aged 35 and over. There are virtually no Bangladeshi women married to non-Bangladeshi men (Diamond & Clarke, 1989; Berrington, 1996; Eade et al., 1996a). However, such patterns may begin to change as communities become more integrated in Britain. Already trends towards increasing bilinguality and socialising with other groups can be observed among women who have spent more time in the UK, and have been exposed to the educational system.

The frequency of visits to a white household can be used as an indicator of migrant integration with the host culture. As expected, second generation women who have gone through the British educational

system and have been more exposed to non-Bangladeshi ways are more likely to make visits to white households than their first generation peers (26% vs. 16% for second and first generation, respectively). Women confided that because of food restrictions (*halal*), these visits rarely included eating a meal. For the same reason, women mentioned that they are more likely to meet their white friends at a café or a restaurant than at their homes.

The ethnic background of women's friends' can also be used as another measure of integration. Adult migrants are more likely to socialise exclusively with Bangladeshi friends than child migrants or second generation women (70%, 31% and 29%, respectively). The younger generations were more likely to have friends of mixed ethnic backgrounds. Very few women (3%) reported having only white friends. The preference among adult migrants for Bangladeshi friends may be a cause and consequence of their limited English skills and movement outside their community.

The type of activities enjoyed during leisure hours is another interesting indicator of the changes taking place among younger migrants living in the UK. Sylheti society, although traditional and observant of Islamic tenets, does not have a strong purdah system, and women have more freedom to move around compared to other Muslim countries. Nevertheless, women in Sylhet are often accompanied in the streets, are escorted during the evening, and if out at this time, are usually in transit. Most social activities occur indoors at relatives' and friends' homes. In accordance with these cultural mores, Sylheti women and adult migrants are more likely to spend their free time at home engaged in sedentary activities, while child migrants and second generation women spend their time equally outside their homes, socialising or shopping. White women, for their part, are more likely to be outside than inside the home, socialising in public places or engaged in physical activities such as dog walking, gardening, etc.

Language skills

Parents of women in all migrant groups still use Sylheti as their mother tongue. Sylheti is a dialect derived from the Bengali language and is almost exclusively spoken in Sylhet District along with standard Bengali for more formal occasions. All adult migrants in the groups under study here considered Sylheti as their mother tongue; the proportion of women who did so among child migrants (79%) and second generation women (47%) decreased as the proportion of bilingual speakers increased. The fact that close to half of second generation women considered Sylheti as their mother tongue despite having been born and educated in the UK suggests that Bangladeshi migrants attach a strong value to their language.

Adult migrant women seem to maintain the exclusive use of Sylheti when speaking to other adults and children in their homes. Child migrants and second generation women tend to use Sylheti and English equally. The prevalence of bilingual households is high among second generation women (80%) and, to a lesser extent, among child migrants (62%); the continued use of Sylheti may be due to the fact that many of the women from these groups are either married to men who speak little English or still have parents with restricted English. The smaller proportion of women who use English exclusively (15%) tend to be women married to men brought up in the UK. Participants often expressed that maintaining use of the Sylheti language was important for communicating with relatives when travelling to Bangladesh.

While most child migrants (89%) and second generation (88%) women speak Sylheti fluently, the ability to read and write Bengali is rapidly lost after migration, with less than half (43%) of second generation women being literate in Bengali. The proportion of women reading and writing Bengali was higher among child migrants (65%), presumably because many of the women in this group had been partly educated in Bangladesh before arriving in the UK. The need to read and write

Bengali is evidently becoming less paramount for British-Bangladeshis. Instead, many children attend after-school Arabic classes in preparation for reading the Koran (Brooker, 2003a).

The self-assessed command of English was, on average, limited among adult migrants (only 40% rated their English as good). Furthermore, fluency of spoken English did not consistently improve with time spent in the UK since migration. This suggests that adult migrant women remain enclosed in their communities, and that their participation in the host country's activities is very limited. This maintains a self-perpetuating situation of exclusion.

Summary

The overall figures obtained in the present study conform to the demographic and socio-economic patterns that have been described for the Bangladeshi community in the UK (Eade *et al.*, 1996a); namely, large family sizes with a very high proportion of young people, low socio-economic status, high dependence on local authority housing, low levels of education attainment and a high proportion of unskilled employment. However, a cross-generational analysis revealed variation within the community with respect to some of these patterns. The results outlined in this chapter show important differences in several socio-economic indicators between overseas and UK-born migrant groups that reflect their different degrees of acculturation and social integration. Specifically, among the British-born groups there are signs of a shift toward nuclear, smaller and less crowded households, wider house tenure and social and economic mobility. In relation to issues concerning women, there is evidence for higher educational attainment and employment and, along with this wider participation in economic activities, larger financial responsibilities in the family. Similarly, there is evidence of changes in marital patterns and social interactions away from traditional norms. From the data presented here, it would appear

that among the new generations, the roles and situation of women in the Bangladeshi community are changing in a more radical way than those of their male counterparts. Such transformations are likely to have far-reaching consequences not only for issues related to family dynamics; but also for reproductive decision-making, lifestyles and, ultimately, women's health. Thus, the results of the present study extend beyond sociological interest and may be relevant for issues of public health, specifically those concerned with ethnic minorities.

CHAPTER 3

Betel nut use among first and second generation Bangladeshi women in London, UK

Introduction

Betel nut is a common masticatory drug used daily by over 600 million people worldwide (Warnakulasuriya, 2002). Originally endemic to South and Far East Asia and Melanesia, the practice has accompanied Asian migrants to countries in the West (Gupta & Warnakulasuriya, 2002).

In different cultures betel is regarded as a general tonic for its physiological and psychological effects. It has been used in folk medicine as an antiseptic and painkiller as well as a basic ingredient in the traditional treatment of mental disorders (Williams, 1995). Consumers cite many reasons for chewing betel, among these: the capacity to strengthen the gums and sweeten the breath, control diarrhoea and vomiting, remove intestinal helminths, relieve toothache, satisfy hunger, promote digestion, to overcome the boredom and monotony of work and for its euphoric effect (Schonland & Bradshaw, 1969; Mehta *et al.*, 1971; Chandra *et al.*, 2003). Women claim that when taken in the first trimester, betel quid provides relief from pregnancy-related nausea (Williams, 1995).

Some of the claimed benefits of chewing betel nut have been supported by scientific evidence (Johnston *et al.*, 1975; Sitaram *et al.*, 1978; Howden, 1984; IARC, 1985; Frewer, 1990; Taylor *et al.*, 1992; Chu, 1994, 1995; Asthana *et al.*, 1996), while other research has highlighted a variety of negative health outcomes. There is evidence for betel nut having goitrogenic (Van der Bijl & Thompson, 1998) and diabetogenic properties (Mannan *et al.*, 2000; Boucher & Mannan, 2002). It has been

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implicated in aggravating cardiac diseases in susceptible patients (Deng *et al.*, 2001), increasing the risk of cirrhosis (Tsai *et al.*, 2003), provoking bronchospasms in asmathics (Taylor *et al.*, 1992; Nelson & Heischober, 1999) and causing adverse pregnancy outcomes (Yang *et al.*, 1999; Yang *et al.*, 2001). Studies have also identified a number of carcinogenic and antioxidant properties of the betel nut which have been implicated in the development of oral and foregut carcinoma (Thomas & Maclennan, 1992; Babu *et al.*, 1996; Sharan, 1996; Chaudhry, 1999; Pearson *et al.*, 2001; Phukan *et al.*, 2001; Zain, 2001; Sharma, 2003).

Research on various Asian ethnic groups resident in the Western world has shown that the consumption of areca nut (often mixed with smokeless tobacco) is widespread in these communities (Pickwell *et al.*, 1994; Winstock *et al.*, 2000; Warnakulasuriya, 2002). Following the importation of this habit to the new countries of residence, betel nut use may be reinforced by the perception of it as a tradition to be valued and retained as part of an overall cultural identity (Williams, 1995). In the UK in particular, studies have revealed a very high prevalence of betel chewing among both sexes and all age groups, but with a significant bias towards female users, and an increased incidence with age (Summers *et al.*, 1994; Williams *et al.*, 1995; Bedi, 1996; Shetty & Johnson, 1999). The practice is often acquired at very young ages (as early as 5) but typically in the early teenage years (Bedi, 1996; Osman *et al.*, 1997; Prabhu *et al.*, 2000; Farrand *et al.*, 2001).

The widespread habit of betel nut use has raised concern among public health authorities because of its adverse health effects. In particular, there is an elevated risk of oral and oesophageal cancers amongst betel-chewing Asian immigrants living in the UK (Chaudhry, 1999; Pearson *et al.*, 2001; Sharma, 2003) and a potential diabetogenic effect (Mannan *et al.*, 2000; Boucher & Mannan, 2002) in a population with an already high incidence of Type 2 diabetes (Nazroo, 1997; Ridge *et al.*, 2001; Unit, 2001; Sayeed *et al.*, 2003). Of further concern is the capacity of betel nut

to be psychologically addictive and cause dependency syndrome (Winstock *et al.*, 2000). An aggravating factor is the perception among members of South Asian communities that betel nut chewing, both with and without tobacco, is beneficial and socially acceptable (Bedi, 1996) and unassociated with cancer or other health risks (Shetty & Johnson, 1999). Such attitudes are reinforced and perpetuated by the recent increase in the availability and variety of the different betel products in the UK market elicited by the demands of a growing Asian community. In East London alone, the revenue from betel nut sales has been estimated at approximately one million pounds sterling per year (Williams *et al.*, 1995; Croucher & Islam, 2002).

Among Asian communities in the UK, empirical evidence suggests that Bangladeshis are particularly likely to retain the habit of chewing betel nut, possibly due to the more rural background of these migrants (Bedi & Gilthorpe, 1995). As a result, there has been an increasing effort to document the social aspects of betel-quid and tobacco use in this group (Summers *et al.*, 1994; Williams *et al.*, 1995; Bedi, 1996; Shetty & Johnson, 1999; Prabhu *et al.*, 2000; Farrand *et al.*, 2001; Croucher & Islam, 2002). Although there have been surveys that include young age groups (16-35 yrs) (Summers *et al.*, 1994; Bedi, 1996), these have not made the clear distinction between UK-born and Bangladesh-born users. As a result, only inferences about changing patterns in betel-nut consumption between generations have been made to date.

Capitalising on the information obtained as part of the main hormonal focus of this thesis, this chapter presents a descriptive analysis of betel nut use among first and second generation Bangladeshi women of reproductive age living in London. These results can serve as a starting point for future, more comprehensive investigations into the ongoing changes in betel nut chewing practices among South Asian ethnic minorities in the UK.

Methods

Subjects and data collection

The information on betel nut use analysed here was obtained from the health section of the general questionnaire applied to all participants in the hormonal study (see Appendix A for originals). For details on the recruitment protocol refer to Chapter 1.

One hundred and forty-six first and second generation Bangladeshi migrant women aged 18-39 were divided into three groups according to their place of birth and age at migration to the UK:

1) Women born in Bangladesh who migrated to the UK as adults currently resident in London (n=62)

2) Women born in Bangladesh who migrated to the UK as infants or children currently resident in London (n=50)

3) British-Bangladeshi women born and raised in the UK and currently resident in London (n=34)

Statistical analysis

Chi-square tests were used to examine differences in the prevalence of betel nut use among first and second generation women according to occupation (housewives, employed or students), marital status (married or non-married), main language used (Sylheti, English or bilingual) and neighbourhood of residence in London (East London, Camden and Greater London). General Linear Models were used to evaluate the effect of length of exposure to the host culture (number of years in the UK) and age at migration to the UK on betel nut use among first generation migrants (adult and child migrants), as well as the effects of age and years of education on betel nut consumption in all three groups.

Statistical analyses were performed using SPSS 10.0 for the Macintosh. The significance level was set at p<0.05.

Results

Betel nut use prevalence was 22%, 33% and 32% for adult migrant, child migrant and second generation groups, respectively; no significant difference was found between groups (χ^2 = 2.18, df = 2, p = 0.33). However, betel nut users were significantly older than non-users (F = 17.07, df = 1, p<0.001) in all groups but particularly among first generation adult women for whom the age difference between users and non-users was greatest (6.5 yrs vs. 0.5 in child migrants and 2.4 second generation women) (F = 5.4, df = 2, p<0.01). Similarly, betel quid users were significantly less educated than non-users in all groups (F = 4.8, df = 1, p = 0.03) (Table 9).

There was no significant effect of either length of time living in the UK on betel nut use among first generation women (F = 0.02, df = 1, p = 0.86) or of age on arrival (F = 0.45, df = 1, p = 0.50) even after controlling for current age.

No significant differences were observed in the prevalence of betel nut use among women speaking different languages (χ^2 = 2.52, df = 2, p = 0.28). Of all betel nut users, 61% spoke Sylheti, 36% were bilingual and 3% spoke English in the home; the proportions for non-users were 62%, 28% and 10% respectively. No differences in betel nut use prevalence due to occupation (χ^2 = 3.50, df = 2, p = 0.17), marital status (χ^2 = 0.001, df = 1, p = 0.97) or borough of residence (χ^2 = 4.90, df = 2, p = 0.09) were found.

Table 9. Average age and years of education among users and non-users of betel nut by migrant group

	GROUP			
	ADU	*CHI*	*2ndGEN*	*All groups*
AGE (yrs) (X ± SE)				
NON-USER	30.6 ± 0.7	27.6 ± 0.7	23.8 ± 0.7	28.2 ± 0.5
n	47	32	23	102
USER	37.1 ± 0.6	28.1 ± 1.12	26.2 ± 1.1	30.4 ± 0.9
n	13	16	11	40
EDUCATION (yrs) (X ± SE)				
NON-USER	9.9 ± 0.6	13.0 ± 0.6	14.4 ± 0.5	11.9 ± 0.4
n	46	32	23	101
USER	8.2 ± 1.0	12.7 ± 0.7	13.3 ± 0.6	11.4 ± 0.6
n	13	16	11	40

Discussion

Characteristics of the study sample

The socio-economic indicators included in this analysis (years of education and employment) suggest that women born in the UK and those who arrived in England as children have had more years of formal education than women who arrived as adults. Second generation women and to a lesser extent child migrants, are English speakers and are more likely to be employed. As a consequence, they are more likely to be exposed to the host culture, and better at negotiating local systems and services effectively. Adult migrants in contrast, especially those who arrived in the UK at later ages, have fewer language skills and are, therefore, less likely to be employed. As a result, they are less exposed to British customs.

Betel nut use

The lack of significant differences in betel nut use between first and second generation migrants in London is unexpected. It was predicted that women brought up in a social environment, such as the British school system where betel nut chewing is not practiced and even discouraged, would be less likely to embrace the habit. However, compared to previous surveys where betel nut use prevalence has been found to be in the range of 60-95% (Summers *et al.*, 1994; Bedi, 1996; Ahmed *et al.*, 1997), the prevalence of 22-33% among the three migrant groups here is considerably lower. Although not statistically significant, adult migrants have the lowest prevalence of use (21.7%).

There are various possible explanations for these findings: first, the eligibility criteria for the hormonal study were aimed at maximising the measurement of steroids, and therefore restricted the sample to women of reproductive age (18-39 years old). This age range is considerably narrower than other studies on betel nut chewing among Bangladeshis

in England, and does not include the age group >45 yrs where prevalence is highest (65-85%) (Bedi, 1996; Shetty & Johnson, 1999). Our findings that betel nut users in all groups are significantly older than non-users support the notion of a lower prevalence use among younger women. The age difference between users and non-users was also greater among adult migrants. This suggests that even women brought up in Bangladesh, where betel nut use is widely accepted and encouraged, are amenable to changes in attitudes regarding betel nut practice.

Another feature of the adult migrants included in the present sample is that they were recruited almost entirely at local community centres and schools where active programmes on health awareness regarding betel nut consumption are in place. It is therefore possible that the individuals sampled were inadvertently biased towards low betel nut use.

A further aspect of this study that may have influenced our results is that it was conducted in London. The Bangladeshi communities in Tower Hamlets and Camden, although still very much adhering to traditional and religious values, are presumably more exposed to the cultural, idiosyncratic and economic diversity characteristic of the Capital than communities in Aston and Yorkshire, where previous studies have been conducted (Summers *et al.*, 1994; Williams *et al.*, 1995; Bedi, 1996). Bangladeshis in the latter areas may be more isolated and there may be a stronger need to maintain a distinct identity through culturally accepted practices such as betel nut chewing. A higher prevalence of the habit could therefore be expected in these communities compared to London.

To further explore the effect of a particular social and cultural environment on the prevalence of betel nut use, comparisons were made between women living in two different communities within London: Tower Hamlets is the oldest focus of Bangladeshi settlement, and is a large, well established community, with purpose-built mosques and a

variety of retailers and services that cater for the religious and dietary needs of Bangladeshis, who comprise the largest ethnic group in the Borough (Carey & Shukor, 1985; Eade *et al.*, 1996b). Camden, in contrast, is a more recent, smaller and less geographically contained community, with fewer shops and services for the Bangladeshis, who represent only one of the many ethnic groups in the Borough (Brooker, 2003b). The results fail to show a difference in betel nut use between these two particular communities, although this may be due to the small sample size. More than just focusing on prevalence, it would be useful in future studies to analyse in more detail the perceptions, beliefs and practicalities maintaining the habit of betel nut use in both communities.

Another factor likely to influence the maintenance of betel chewing among migrants is the degree to which women have been exposed to mainstream British society. We have used four possible approaches to measuring acculturation among the Bangladeshi sample in the UK, namely length of time spent in the UK since migration, age at migration, occupation, and language spoken at home. None of these variables show a statistically significant relationship with betel nut use, although English speakers were less likely to be betel chewers. Again, lack of statistical significance may be due to the small sample sizes of this study. The low betel nut use among women who choose to speak English as opposed to Sylheti in the privacy of their home suggests that this practice may be in decline. The use of the host culture's language (mostly by first generation migrants who arrived as children and second generation women) may also reflect to some degree, the acquisition of values and beliefs that make the habit of chewing betel nut seem inappropriate. In support of this idea, education measured as number of years of schooling does have a significant effect on betel nut use, irrespective of the country of school attendance: less educated women are more likely to be betel nut chewers. This could reflect different socio-economic status, rural versus urban background, and/or differences in

knowledge and awareness regarding betel nut risks inherently linked to education status.

In summary, the findings of this study show a lower prevalence of betel nut use among first and second generation Bangladeshi women than previously reported. Although there are some indications of a change in behaviour among younger individuals, the data also show that betel nut chewing is a practice very much present among women born and brought up in a bicultural context. This speaks of the importance of chewing betel nut for Bangladeshis, and of the strong influence the family and immediate community have on maintaining this behaviour. However, the present study did not explore the beliefs and perceptions regarding betel nut use held by members of different age generations. It is therefore difficult to speculate on the reasons for retaining a habit that has proven deleterious for health. Further work on these lines is indispensable to inform the planning of effective community health programmes aimed at decreasing betel nut chewing among Bangladeshis living in Britain.

CHAPTER 4

The effect of chewing betel nut on measurements of salivary progesterone and oestradiol.

Introduction

The development of steroid salivary assays has expanded the scope of sampling regimes in endocrinology as well as field-based research in reproductive ecology. This non-invasive, simple way to obtain whole menstrual cycle profiles of progesterone and oestradiol has revolutionised the study of the factors that impact ovarian function (Read et al., 1986; Riadfahmy et al., 1987; Ellison, 1994) and has allowed comparisons among populations living in a variety of ecological settings (Ellison & Lipson, 1999). Furthermore, the ease with which salivary samples can be collected makes this technique an excellent option for the measurement of steroids in clinical research (Haeckel & Hanecke, 1993; Voss, 1999; Lac, 2001).

Many populations, however, observe cultural practices that could potentially hamper accurate hormonal analyses using saliva (e.g., (Vitzthum et al., 1990). One such practice is betel nut chewing, endemic to the Indian sub-continent, Southeast Asia and large parts of the western Pacific, as well as among migrants from these areas to other countries. It has been estimated that 10-20% of the world population engage in this habit (Boucher & Mannan, 2002; Strickland, 2002; Warnakulasuriya, 2002). The aim of this part of the study was to evaluate the effect of betel chewing on the accurate measurement of salivary reproductive steroids using radioimmunoassay (RIA) to assess whether the feasiblility of using this technique in a betel-nut chewing population. It was conducted as a pilot, preparatory to a larger investigation on the effects of migration on reproductive hormone levels among Bangladeshi women in the UK.

Betel chewing has been practised for centuries, and is firmly rooted in the social, cultural and economic life of many populations (Strickland, 2002). In some regions, however, perceptions are beginning to change, and people with coloured teeth resulting from heavy betel chewing are now more likely to be deprecated. The practice of chewing betel nut, nevertheless, is still widely regarded as socially acceptable, and in most countries is supported by positive marketing strategies as well as legal distribution (Croucher & Islam, 2002; Gupta & Warnakulasuriya, 2002).

While the constituents of betel chewing may be consumed separately or in various combinations, the most commonly described form is the "quid". The ingredients in the betel quid (also known as *paan* for its name in Hindi) vary depending on geography, local custom, and personal preference, but the major components are betel nut (*Areca catechu*), betel leaf (*Piper betel*), slaked lime (calcium carbonate) as an alkaloid enhancer, and "catechu" an astringent extract of the wood *Areca catechu*. Smokeless tobacco leaf (either *Nicotina tobaccum* or *Nicotina rustica*) is a common additive along with other spices and flavourings such as aniseed, fennel and coriander seed (Williams, 1995; Bedi, 1996; Strickland, 2002). The quid can be made up at home or purchased ready-made. Generally, lime and catechu are smeared on a betel leaf, which is then partially folded into a funnel shape into which the small pieces of betel nut and the rest of the ingredients are added. Once folded completely, the resulting quid is placed in the mouth -- usually in the cheek -- and gently chewed and sucked. The quid may be stored in the buccal mucosa for varying periods of time, ranging from 5-60 minutes, or even overnight. Chewing encourages salivation, and the practice produces red saliva which discolours the teeth and lips. After chewing, the quid may be swallowed, or more often, saliva and quid are expectorated.

Estimates differ concerning how many quids are chewed daily, and can range from 1-15 or more; veteran chewers may consume up to 30 quids

per day. Chain chewing occurs, particularly when tobacco is included as an ingredient (Sankaranarayanan, 1990; Summers *et al.*, 1994). The betel chewing mixture without tobacco is claimed to be a mild stimulant and addictive agent (Burton & Burton-Bradley, 1979); heavy chewers may present withdrawal symptoms (Capdevielle-Pardies *et al.*, 1984; Winstock *et al.*, 2000).

Methods

Study population

Twenty Bangladeshi women living in London, UK, aged 18-42 and regular users of betel quid were recruited into the study. Women were contacted through bilingual link workers at local schools and community centres and invited to participate in the study. After obtaining written informed consent, women were screened for steroid-contraceptive use, menstrual cycle irregularities, infertility, diabetes, and thyroid disorders that might affect their steroid hormone profiles. On the day of saliva collection, a 15-minute questionnaire on betel-nut use, reproductive, medical and migration histories was administered by a bilingual (English-Sylheti) female research assistant. Heights and weights were obtained following standard anthropometric procedures (Gibson, 1990) (see Appendix C).

Sample collection and analysis

To maximise potential levels of both progesterone and oestradiol, women were scheduled to participate in the pilot study during the mid-luteal phase of their menstrual cycle. Based on the date of their previous menses and on the reported average length of their menstrual cycles, participants took part in the study between eight and ten days prior to the estimated date of their subsequent menstrual period. Participants were followed up to obtain the exact date of their subsequent menses, and to calculate retrospectively the actual luteal day on which the samples were

collected. Menstrual cycle days were then numbered in reverse counting backwards from the subsequent first day of menstruation, such that the last day of the menstrual cycle during which saliva was collected would be counted as Day −1. Samples outside the luteal phase (<-14 reverse menstrual day) were only assayed for oestradiol. Two pregnant women in their third trimester with presumed high reproductive steroids levels were also included in the sample.

Women were requested to refrain from chewing betel nut from the evening preceding the study, and not to eat, drink (except water) or brush their teeth (in case of bleeding gums which might contaminate the saliva sample) for a minimum of one hour prior to sample collection.

During the study, participants were asked to prepare their customary betel quid using their own ingredients and to chew as normal. It took them between 5 to 15 minutes to finish the betel quid. Some women spat out the debris while others swallowed it.

Collection schedule

All saliva samples (5 ml) were collected in the morning according to the following schedule:

> Sample 1: Collected immediately prior to chewing the betel quid (baseline levels).
>
> Sample 2: Collected immediately after finishing chewing the betel quid.
>
> Sample 3: Collected 30 min after sample 2.
>
> Sample 4: Collected 60 min after sample 2.
>
> Sample 5: Collected 120 min after sample 2.
>
> Sample 6: Collected 240 min after sample 2.

Participants were allowed to drink water during the study. Only three women consumed food (between samples 5 and 6), but finished eating on average 90 minutes prior to Sample 6 collection.

Saliva samples were collected, stored and assayed using standardised radioimmunoassay techniques described previously (Lu *et al.*, 1997, 1999), and detailed in Appendix D. All samples had comparable handling and treatment conditions and were assayed simultaneously within two months of collection. Previous work has demonstrated that treating samples with sodium azide (0.1 g/L) allows storage at ambient temperatures for up to six months thus preventing sample degradation and significant distortion of results (Ellison, 1988; Lipson & Ellison, 1989b). Samples from a given individual were run in the same assay to minimise the effects of interassay variability. Interassay variability averaged 39.9 % for progesterone and 34.1% for oestradiol, and intraassay variability averaged 13.2% for progesterone and 13.4% for oestradiol. The sensitivity limit of the assay was 31 pg/ml for progesterone, and 1.56 pg/ml for oestradiol.

Participants were divided into 3 categories according to the frequency of use of betel nut: low (<3 quids/day), medium (3 quids/day), high (>3 quid/days).

A univariate repeated measures analysis (GLM with Huynh-Feldt correction) was used to evaluate whether there was a short-term effect of chewing betel nut on the measurement of salivary progesterone and oestradiol. Sample number was entered as a within-subject factor to assess variation relative to individual baseline levels while age, chewing frequency and the presence of two ingredients (tobacco and lime) were entered as between-subject factors.

Statistical analyses were performed using SPSS v. 10.0 for the Macintosh. The significance level was set at $p < 0.05$.

Results

Of the original 20 participants, only those with hormone levels above the limits of assay detection were included in the analyses (n = 12 and n = 13 for progesterone and oestradiol, respectively). Tables 10 and 11 present the individual raw levels (pg/ml) for each steroid for each point in the time series (samples 1-6). Average steroid levels for each sampling interval are summarised in Figures 2 and 3.

Results for within-subject variation were not significant for either progesterone (F = 0.98 df = 2.19, p = 0.39) or oestradiol (F = 1.07, df = 1.76, p = 0.35). Steroid variation over time (samples 3 through 6) was not significant even after age, chewing frequency, tobacco and lime use were added as between-subjects factors. None of the interactions were statistically significant.

Table 10. Time series experiment on the effects of betel nut chewing on the measurement of progesterone in saliva.

N	DAY OF SAMPLE COLLECTION (REVERSE MENSTRUAL DAY)	SAMPLE No. / TIME RELATIVE TO CHEWING BETEL NUT						
		1 (Immediately before)	2 (Immediately after)	3 (30 min after)	4 (60 min after)	5 (120 min after)	6 (240 min after)	(X ± 95%CI)
		Raw salivary progesterone levels (pg/ml)						
Low frequency chewers (<3 quids/day)								
1	-9	77.5	145.2	89.0	47.7	106.7	127.8	95.6 ± 29.8
2	-8	101.3	204.6	60.0	108.2	64.7	139.3	113.0 ± 42.9
3	-7	48.3	9.0	42.1	64.0	71.1	97.3	55.3 ± 23.9
4	-6	37.2	68.0	39.5	51.8	28.6	62.6	47.9 ± 12.3
5	-5	28.3	0.0	6.7	0.0	0.3	0.0	6.1 ± 9.4
6	pregnant	219.5	137.2	131.8	111.6	189.4	192.3	163.6 ± 34.1
Medium frequency chewers (3 quids/day)								
7	-6	31.6	124.5	42.0	30.7	46.8	41.6	52.9 ± 28.6
8	-5	26.8	82.0	45.1	30.3	7.0	40.0	38.5 ± 20.0
9	-5	21.3	5.8	2.2	0.0	13.8	14.9	9.7 ± 6.7
10	pregnant	280.4	138.7	252.1	338.3	307.2	300.2	269.5 ± 56.3
High frequency chewers(> 3quids/day)								
11	-11	84.1	18.6	95.4	55.2	66.6	94.9	69.1 ± 23.5
12	-8	42.0	46.1	44.3	54.7	39.8	78.1	50.8 ± 11.4
	(X ± 95%CI)	83.2 ± 46.8	81.6 ± 38.2	69.2 ± 38.2	74.4 ± 51.0	78.5 ± 50.0	99.1 ± 47.4	

Table 11. Time series experiment on the effects of betel nut chewing on the measurement of oestradiol in saliva.

N	DAY OF SAMPLE COLLECTION (REVERSE MENSTRUAL DAY)	SAMPLE No. / TIME RELATIVE TO CHEWING BETEL NUT						
		1	2	3	4	5	6	(X ± 95%CI)
		(Immediately before)	(Immediately after)	(30 min after)	(60 min after)	(120 min after)	(240 min after)	
		Raw salivary oestradiol levels (pg/ml)						
Low frequency chewers (<3 quids/day)								
1	-21	5.1	2.6	4.8	5.3	5.6	5.6	4.9 ± 3.9
2	-17	7.7	5.8	3.1	3.6	3.1	2.4	4.3 ± 3.5
3	-9	2.2	0.8	3.2	2.1	2.4	1.7	2.1 ± 1.6
4	-5	4.2	6.8	4.1	4.4	3.6	3.4	4.4 ± 3.5
5	pregnant	200.0	86.9	180.7	122.4	133.8	85.3	134.9 ± 38.0
Medium frequency chewers (3 quids/day)								
6	-13	6.8	1.2	1.9	1.8	1.1	1.1	2.3 ± 1.8
7	-6	3.2	4.4	3.6	2.2	2.5	3.3	3.2 ± 2.5
8	-5	2.8	7.4	5.1	2.5	5.7	4.1	4.6 ± 3.7
9	-5	3.4	3.4	1.6	2.4	2.3	4.0	2.8 ± 2.4
10	pregnant	79.1	55.7	100.9	122.4	53.8	81.4	82.2 ± 65.9
High frequency chewers (>3 quids/day)								
11	-23	2.6	9.4	1.9	2.0	1.5	1.6	3.2 ± 2.5
12	-16	10.5	15.7	7.0	10.7	11.2	8.7	10.6 ± 8.4
13	-7	4.7	9.4	5.9	5.2	5.1	4.5	5.6 ± 4.7
(X ± 95%CI)		25.6 ± 30.6	16.1 ± 13.9	24.9 ± 29.4	22.1 ± 24.3	17.8 ± 20.4	16.0 ± 16.3	

Figure 2. Average salivary progesterone levels (pg/ml) for samples collected immediatel before and after betel quid consumption and then 30, 60, 120 and 240 min later.

Time relative to chewing betel quid

n=12

Figure 3. Average salivary oestradiol levels (pg/ml) for samples collected immediately before and after betel quid consumption and then 30, 60, 120 and 240 min later.

Time relative to chewing betel quid
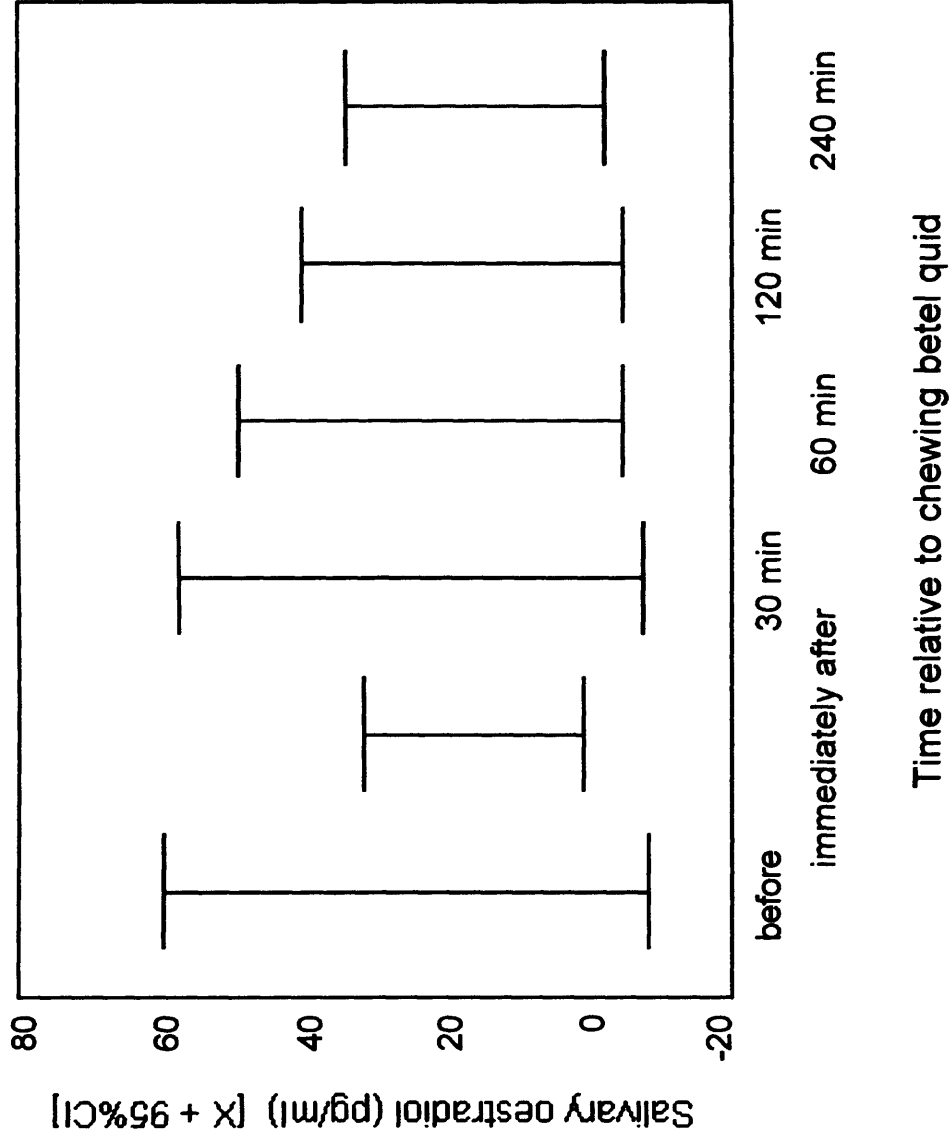
n=13

Discussion

Observation of the data reveals that, although not statistically significant, the saliva sample given immediately after chewing betel quid generally has either elevated or depressed levels of both hormones relative to the sample given before chewing. The pattern, however, is not consistent across individuals, and may reflect variation in *paan* ingredients, time spent chewing, and/or the frequency of use patterns, but the small sample sizes limits effective analyses of all these variables.

Statistical analyses confirm that although post-chewing steroid levels vary, the variation across time is not significant, even after adjusting for frequency of use and inclusion of tobacco and lime. The cause of the apparent alteration of steroid levels in saliva after chewing betel quid is unknown, but it is likely that some ingredient in the quid interferes with the antibody reaction of the radioimmunoassay.

Variation in steroid levels following betel quid chewing could result from a dilution effect of an increased salivary flow elicited by ingredients in the quid. Betel-chewers have been shown to salivate more than non-chewers upon chemical stimulation, with a flow rate positively correlated with the duration of chewing, although no difference in salivary pH has been observed (Reddy *et al.*, 1971). This suggests that experienced chewers could secrete more saliva leading to a concomitant decrease in enzyme, electrolyte and steroid concentration and contributing to the variation in measured steroids observed among subjects.

Despite the small sample size, this study demonstrated that the effects of betel quid chewing on salivary steroid secretions are transitory. Equivalent results to those of the present pilot, were obtained in another small study with a similar collection protocol conducted by Vitzthum et al. (1990) to assess the effect of chewing coca leaves on salivary steroid secretion among Bolivian women. The limited sample sizes in both studies is the result of the extreme difficulty in obtaining saliva samples

that fall in the appropriate phase of the menstrual cycle when participants are scheduled prospectively by taking their recalled last menstrual date as reference. The inaccuracy between the estimated and the real phase of the cycle following collection renders many of the samples inappropriate for analysis and inevitably translates into an attrition of the original sample.

Nevertheless, the data obtained for the population in question here shows that betel quid chewing does not significantly affect the measurement of salivary progesterone or oestradiol using the techniques outlined here for radioimmunoassay. However, given the highs and lows that follow immediately chewing betel quid we recommend waiting at least one hour post quid chewing before measuring steroids in saliva.

In conclusion, with specific collection protocols that take into account time since chewing, it is possible to undertake salivary steroid analyses in populations among whom the practice of chewing betel nut is endemic.

CHAPTER 5

Salivary progesterone and oestradiol levels in Bangladeshi migrant women in the UK

Introduction

A large body of data collected over the last two decades indicates that levels of adult ovarian hormonal function, measured as average profiles of progesterone and oestradiol, vary significantly within individuals over time, between individuals within populations, and between populations even in the absence of pathology (Ellison *et al.*, 1993b; Ellison, 1995). It is now recognised that some of this variation is associated with constitutional, behavioural and ecological factors. Available research on the sources of variation in ovarian function can distinguish between: 1) "random" variation unassociated with any independent variable, 2) variation associated with age; and 3) variation associated with energetic factors (Table 12).

It should be noted that due to the very low levels in saliva, oestradiol is considerably more difficult to measure than progesterone, and assays for oestradiol in saliva have been developed more recently (O'Rourke & Ellison, 1988, 1993; Lu *et al.*, 1999). Hence there is more information at present concerning variation in progesterone than oestradiol profiles.

Table 12. Sources of variation in ovarian function.

SOURCE OF VARIATION	STUDY DESIGN	MAIN RESULTS	CONCLUSION	REFERENCE
1) Random variation	Comparison of salivary progesterone profiles from consecutive menstrual cycles. Subjects: Boston women of reproductive age within normal ranges of weight for height.	Women tend to have individually characteristic progesterone profiles; the variance between women is approximately three times as great as the variance within women.	Luteal function appears to be fairly integrated within individuals and fairly consistent over time in the absence of other influences.	(Ellison 1988)
2) Variation associated with age	Comparison of salivary progesterone and oestradiol profiles of Boston women of different age groups (18 to 48 years old), of stable weight, within normal ranges of weights for height and not engaged in regular strenuous exercise.	Significant differences in progesterone and oestradiol profiles between age groups.	Ovarian function as a whole follows a parabolic trajectory with age with increasing function lasting until the early to mid-twenties and declining function evident as early as the mid-thirties.	(Lipson & Ellison 1992; O'Rourke & Ellison 1993; Lipson & Ellison 1994)
	Comparison of progesterone salivary profiles between different age groups of women in quite disparate populations, widely divergent in geography, culture, genetic background and basic subsistence economy (namely Boston women, Lese subsistence farmers from the Ituri forest of Zaire, and Tamang agro-pastoralists from the highlands of Nepal).	Significant differences by age group in all three populations, and significant differences in average levels at every age between populations, with no interaction effect which indicates that the age patterns in the three populations are essentially parallel.	The parabolic pattern of age variation in ovarian function seems to be a common feature of human biology. The consistency of the age patterns suggests that it is due to underlying processes of maturation and ageing common to all populations and not to the acute effects of ecological variables that happen to be proportionately distributed by age in all populations.	(Ellison et al. 1993; Ellison 1994)
3) Variation associated with energetics (changes in energy balance or energy flux)				
Related to changes in energy intake:				
a) Associated to voluntary dieting	Well-nourished Boston and German women of reproductive age.	Moderate weight loss (1-2 kg/month) is associated with lower luteal progesterone and oestradiol profiles. Magnitude of weight loss significantly correlated with the relative degree of steroid suppression in the month following that in which the weight loss occurred, indicating a lag time in the full effect of this levels of energetic stress.	Ovarian function is sensitive to energy balance (measured as BMI or body weight change).	(Pirke et al. 1985; Schweiger et al. 1987; Lager & Ellison 1990)

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Table 12. Sources of variation in ovarian function (continued).

SOURCE OF VARIATION	STUDY DESIGN	MAIN RESULTS	CONCLUSION	REFERENCE
Related to changes in energy expenditure:				
a) Associated to self-imposed aerobic exercise	Young Boston and German women under vigorous exercise with increased caloric intake to maintain energy balance.	Lower progesterone and oestradiol levels observed among recreational joggers of stable weight, compared with inactive controls of comparable weight and BMI.	Energy expenditure has a negative effect on ovarian steroids independent of energy balance.	(Shangold et al. 1979; Bullen et al. 1985; Ellison & Lager 1986; Bledsoe et al. 1990; Broocks et al. 1990; Ellison et al. 1998)
b) Associated to ecological factors related to subsistence ecology	Well-nourished rural Polish farm women subject to seasonal variation in workload but with stable body weight.	Lower progesterone levels found during the physically demanding season of agricultural work correlated with the amount of energy expenditure but not with energy balance or energy intake.	Energy expenditure has a negative effect on ovarian steroids independent of energy balance.	(Jasienska & Ellison 1998)
c) Associated to variation in habitual physical activity	Rural and urban Polish women of reproductive age	A negative relationship between habitual physical activity groups (low, moderate, high) and salivary levels of oestradiol.	Even moderate energy expenditure associated with lower ovarian function.	(Jasienska et al. in prep)
Related to changes in energy balance due to changes in both energy intake and energy expenditure				
a) Associated to ecological factors related to subsistence ecology	Marginally nourished Lese horticulturalists of the Ituri forest of Democratic Republic of Congo and Tamang agropastoralist women in the Nepalese highlands subject to negative energy balance due to seasonal food shortage and increased workloads.	Sustained weight loss over a season associated with lower progesterone levels between and within women in both populations. In the Lese, sustained population-wide weight loss is associated with lower oestradiol, a steady decrease in ovulation frequency and ultimately with a decline in conceptions. No comparable effect of seasonal negative energy balance on oestradiol levels among Tamang women.	Reduced luteal function in periods of negative energy balance. Inconsistent results for oestradiol.	(Ellison et al. 1986, 1989; Bentley et al. 1990; Bailey et al. 1992; Panter-Brick et al. 1993; Panter-Brick et al. 1996)
4) Variation associated to nutritional ecology	Western women	Vegetarian and high fiber diets, associated with low levels of oestradiol compared to omnivorous, low fiber diets. Conversely, high fats have been associated with elevated gonadal steroid levels.	Diet composition appears to affect reproductive steroids metabolism.	(Armstrong et al. 1981; Goldin et al. 1982; Goldin et al. 1986; Persky et al. 1992; Barr et al. 1994)

The main points that can be drawn from the current knowledge of variation in adult ovarian function related to energetics are:

• Despite the differences in genetic background, geography, culture and life-style, the patterns of ovarian response to unfavourable energetic conditions observed in all populations studied so far are strikingly similar.

• Human ovarian function does vary with chronic and acute energetic conditions, either voluntarily imposed or ecologically determined; whether related to variations in energy intake, variations in energy expenditure, or a combination of both.

• The responsiveness of ovarian function to energy balance and energy expenditure is finely tuned along a graded continuum ranging from fully fecund cycles with high steroid profiles to the absence of cyclic ovarian activity (chronic amenorrhoea) and temporal infertility. Such responses are reversible upon improvement of energetic conditions (Ellison, 1990).

• Different populations appear to operate at different basal levels of ovarian function and variation due to the acute factors exists *around* that basal level. Such variation is observable even under generally favourable energetic conditions (in affluent populations), and not only limited to situations of chronic undernutrition.

From an evolutionary perspective, the short-term responses of the reproductive system to energy availability can be regarded as adaptive and the product of natural selection rather than a pathological failure of homeostasis. Given the taxing costs of reproduction on the human female (Durnin, 1991; Dewey, 1997; Butte *et al.*, 2001), and the instability and unpredictability of the environment in which modern humans evolved (Lahr & Foley, 1988), a strategy that could balance the competing reproductive and physiological investments in the face of

temporal energetic constraints (due to low intake and/or high energy expenditure) would be expected to yield higher reproductive fitness.

One such strategy is to adjust ovarian function in relation to the fraction of total metabolic energy available to invest in a *successful* reproductive effort. In this way, when energetic conditions are unfavourable, gonadal function is temporarily suppressed, steroid levels lowered and, as a consequence, the probability of conception and/or successful implantation during that menstrual cycle diminished (Eissa *et al.*, 1986; McNeely & Soules, 1988; Lipson & Ellison, 1996): thus the risk of engaging in a costly reproductive event with low probability of success and negative consequences for future reproductive potential is prevented (Ellison, 1990; Peacock, 1991; Vitzthum, 1997). This ovarian suppression contributes to extended periods between successive births and allows for maternal recovery which, in the long-term, avoids the costs of maternal depletion, both for the mother and the surviving offspring (Lechtig *et al.*, 1975; Merchant & Martorell, 1988; Miller *et al.*, 1994; Pike, 1999; George *et al.*, 2000).

Similarly, the parabolic trajectory of ovarian function with age over the lifetime of an individual can be interpreted as adaptive within the framework of life history theory, and arguably, may be partly a function of the relative longevity and prolonged period of parental investment observed in humans, as in other large mammals (Ellison, 1995).

Life history theory builds from the assumption that energy is a limited resource that needs to be partitioned between various life functions: maintenance, growth and reproduction. Decisions about how to invest energy harvested during the life cycle are expected to be driven by natural selection to yield optimal allocation patterns given relevant constraints. Since the energy used for one purpose cannot be used for another, living organisms face a series of trade-offs. The most fundamental of which are the trade-off between current and future

reproduction, and the trade-off between number and fitness of offspring produced (Gadgil & Bossert, 1970; Stearns, 1992; Charnov, 2001).

Predictions of this theory would state that increasing ovarian function with age over the first half of the reproductive career represents a trend of increasing reproductive effort, a shift of resources in the direction of reproduction at a cost of the mother's own maintenance. Increased reproductive effort is predictable as a woman's own reproductive value and the chances of future reproduction decline with advancing age. In mid-reproductive career the trend reverses and ovarian function begins to decline steadily, associated with longer waiting times to conception (Goldman *et al.*, 1987; O'Connor *et al.*, 1998). This shift of resource distribution in favour of maternal maintenance is a consequence of the dependency of children already born on the continued survival of the mother. Moreover, the mechanical constraints related to ageing oocytes and dwindling follicular reserve in the ovaries further diminish the expected fitness of offspring born late in a woman's reproductive career. Thus, the scale is tipped even more in favour of investment in children already born rather than investment in further reproduction.

Inter-population variation in ovarian function

In addition to the variation in ovarian function within individual women from cycle to cycle and the variation between women within a given population associated with age and energetics, there are significant differences between populations in average indices of ovarian function. These inter-population differences are apparent in the comparison of the trajectories of ovarian function by age (Ellison *et al.*, 1993b) and in the composite average progesterone and oestradiol profiles of the widely divergent populations studied so far (Danutra *et al.*, 1989; Bentley *et al.*, 1990; Ellison *et al.*, 1993b; Panter-Brick *et al.*, 1996; Vitzthum *et al.*, 2002) (Figure 4). It appears that in different populations different baseline levels of ovarian function are established and that other patterns of variation, associated with age or energetics for example, are

observable relative to these baselines. Similarly, individual women differ in their characteristic hormonal profiles with individual variation occurring *relative* to these baselines.

Neither the significance nor the aetiology of inter-population differences in ovarian function is well understood. The consistency of the differences in level of ovarian function across different ages makes it plausible that they reflect differences in established features of adult ovarian function rather than acutely generated differences that happen to be proportionally distributed by age. Reproductive ecologists have proposed that such baseline, or chronic variation may be related to developmental factors (Ellison, 1996; Worthman, 1999) and that it occurs as a consequence of differences in chronic energy availability during growth and development. Such differences would then result in diverse maturation tempos and in the establishment of different adult physiological set-points for regulation of the hypothalamic-pituitary-ovarian (HPO) and related metabolic axes (Ellison, 1996; Lipson, 2001; Vitzthum, 2001).

Figure 4. Inter-population variation in progesterone profiles
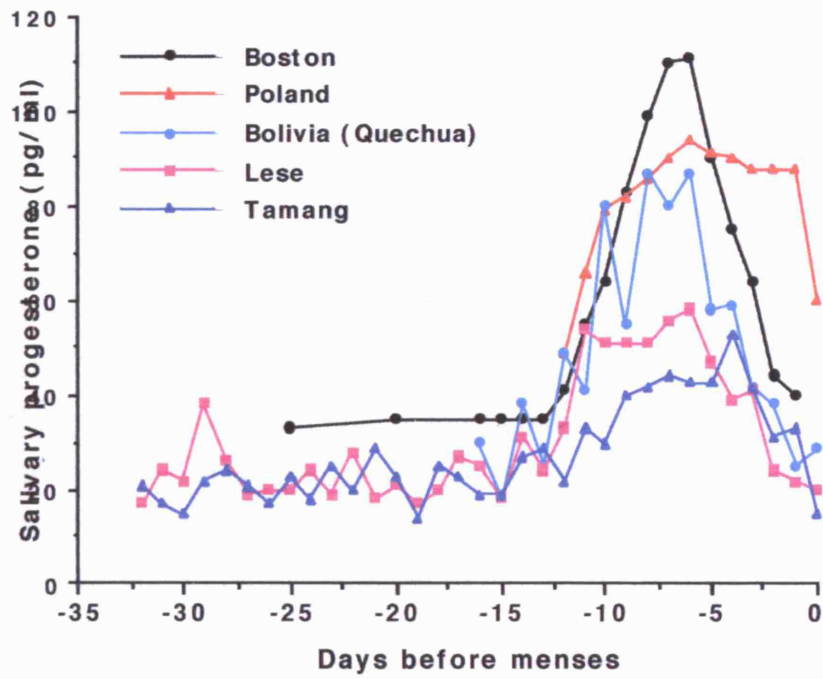
Data reprinted with permission of Boston (Peter Ellison), Grazyna Jasienska (Poland), Catherine Panter-Brick (Tamang), Quechua (Virginia Vitzthum).

Variation in chronic energy availability can be related to nutritional, energetic and epidemiological factors. Most research in the field of reproductive ecology conducted so far, has focused mainly on the first two ((Ellison *et al.*, 1993b; Jasienska, 2001) for reviews), presumably because they have been the most obvious features of the ecology of the populations studied, and partly, because they are somehow easy to measure, either directly or through proxies, such as changes in body weight and composition, energy expenditure indices, and so forth. However, ample evidence points to the epidemiological factor as inexorably linked to chronic energy availability. For instance, it is widely recognised that chronic illness has a negative impact on growth and maturation (Tanner, 1992; Solomons *et al.*, 1997; Moore *et al.*, 2001; Campbell *et al.*, 2003; Panter-Brick *et al.*, 2004). Frequent or chronic diseases provoke persistent stimulation of the body's inflammatory and immune systems with the concomitant lymphocyte proliferation and rise in antibody production. These are processes that are expensive in terms of energy and may result in restricted growth despite adequate food availability (Stephensen, 1999).

Direct reliable measurements of the energetic costs of continuous immune activity and its long-term repercussion on reproductive effort prove very difficult to obtain (McDade & Worthman, 1999; Long & Nanthakumar, 2004). However, the prediction derived from lifetime resource allocation and life history theory (Gadgil & Bossert, 1970; Charnov, 2001) is that the experience of recurrent or chronic illness during childhood should be negatively associated with adult rates of reproduction. In mathematical modelling of life history, a reduction in pre-reproductive mortality results in an acceleration of reproductive maturation, which suggests that this association is of adaptive value (Cole, 1954; Gadgil & Bossert, 1970; Schaffer, 1974). The rationale being that individuals developing in a high morbidity environment would have to trade-off survival at high energetic costs through the maintenance of a chronically stimulated immune function, for a slower

developmental trajectory with restricted growth, late maturation and presumably lower levels of reproductive function.

Empirical epidemiological data confirm the prediction, and show that the secular trend in human maturation finds its closest correlate in the declining mortality rates of the demographic transition (underlain by a dramatic shift in patterns of morbidity); by reducing costs of maintenance of the immune function, energy for growth and reproduction is freed and maturation is accelerated (Ellison, 1981a, b; Eveleth & Tanner, 1990).

As with the case of adjustment of reproductive function to short-term energetic conditions, it has been argued that the *developmental* adjustment of baseline trajectories of ovarian function may also represent a phenotypic adaptive mechanism to adjust adult fecundity and reproductive effort to chronic conditions governing the energy available for growth or reproduction. This notion of developmental plasticity is known in life history theory as reaction norm. Specifically, this concept refers to the range of potential phenotypes that may result from the interaction of a particular genotype and the environmental conditions it finds itself in (Stearns, 1992).

In the model under discussion here, the rate of childhood growth and adolescent maturation would be used as a bioassay and empirical index of the overall level of energy above maintenance costs that is likely to be available to an individual in a particular ecology to be allocated to reproduction (Martorell *et al.*, 1996); such cues would then be used to adjust the *baseline* levels of adult ovarian function to those that would yield maximum lifetime reproductive outcome under such conditions.

From this viewpoint, energetic conditions during development that result in slow growth and delayed reproductive maturation are predicted to lead to *lower* baseline levels of ovarian function and *heightened* ovarian sensitivity to ecological factors, such as weight loss, throughout life.

Because, as mentioned earlier, lower levels of ovarian hormones are associated with a lower probability of conception and/or implantation, these features would result in a highly conservative reproductive strategy of lower lifetime fecundability, fewer pregnancies and increased average inter-birth intervals (Ellison, 1991). The adaptive value of this strategy lies in that, by helping individuals maintain long-term energy balance in chronically energetically hostile environments through reduction of reproductive costs, it would increase their survival and ultimate fitness (Ellison, 1996; Lipson, 2001; Jasienska, 2003). The increase in lifetime reproductive fitness is brought about not through increased fertility, but by increasing the probability of maternal survival and consequently, that of her already born offspring through enhanced investment. This is particularly important for humans as a species given the prolonged period of childhood dependency on parents, the longest of all mammals (Blurton-Jones & Sibly, 1976).

An alternative to this adaptive explanation for the chronic suppression of ovarian function under conditions of poor energy availability is the possibility that such low levels of reproductive function are in fact, pathological; that stressful energetic conditions during development cause physiological systems, including the reproductive system to run below an "optimal". This view, most often adopted by clinicians implies that there is a "normal" level of ovarian function -- that of contemporary healthy Western women who enjoy optimal conditions of food availability, access to medical care and low physical exertion, and that any departure from it is "dysfunctional". However, the conditions of energy surplus enjoyed by these Western women are quite unusual in our species' evolutionary history and, indeed, very different from those in which modern humans evolved. Therefore, it might be that the "suppressed" ovarian function observed under conditions of limited energy availability has actually been the usual condition for human populations, and therefore more likely the product of natural selection (Ellison, 1996; Lipson, 2001; Jasienska, 2003). Unfortunately, because

of the difficulty entailed in collecting the appropriate longitudinal and trans-generational data needed, empirical tests of the adaptive value of variation in chronic levels of ovarian function in terms of Darwinian fitness are still lacking.

Regardless of the functional meaning of the existing inter-populational variation in ovarian function, there is evidence in support of the idea that such variation is determined by developmental conditions. For instance, the association between age at menarche (proxy for maturation tempo) and levels of ovarian function has been demonstrated within and between populations. In particular, data indicate that early reproductive maturation is associated with a pattern of higher ovarian steroid secretion and higher reproductive function compared to later maturation. For example, in a longitudinal study that followed girls from pre-puberty to adulthood, early maturers had a greater prepubertal rise in serum oestradiol concentrations, higher oestradiol levels in adulthood and a faster pubertal development which included a more rapid onset of ovulatory and luteally sufficient cycles (Vihko & Apter, 1984; Apter & Vikho, 1985; Apter, 1996). Other reports in American (Gardner, 1983; Gardner & Valadian, 1983) and Italian (Venturoli et al., 1987) women have documented a higher incidence of ovulatory failure and other menstrual problems in late maturing girls compared to those with an early menarche. A large cross-sectional study of women of reproductive age from 12 different populations found an inverse relationship between age at menarche and urinary follicular oestrogen levels (MacMahon et al., 1982). Similarly, mean luteal progesterone levels of women from five different populations living in various energetic conditions (middle-class women in Boston, rural farmers in Poland, Quechua women in Bolivia, Lese horticulturalists in the Ituri forest of Zaire and Tamang agro-pastoralists in Nepal) show a negative relationship with the mean reported age at menarche for each respective population (Ellison, 1996). The association between developmental conditions and levels of ovarian function finds further indirect support in work that demonstrates that

energetic conditions affect menarcheal age. For example, it has been noted for a long time that female competitive athletes and ballet dancers have a delayed menarche compared to their non-athletic counterparts (Malina et al., 1978; Warren, 1980; Frisch, 1987). Similarly, observations in American girls indicate that a weight-for-height one third greater than normal is correlated with earlier menarche (Garn & Haskell, 1959; Zacharias et al., 1970). At an epidemiological level, weight gain during childhood has been found to affect age at menarche: in a study of British girls, investigators found that the heaviest girls at age seven had a significantly earlier age at menarche than the lightest girls (Cooper et al., 1996).

The above evidence considered together suggests that energetic conditions conducive to early reproductive maturation (presumably energy abundance) could be associated with a pattern of high adult levels of ovarian steroid secretion. Conversely, situations leading to late maturation result in low set points of ovarian hormones. However, although this evidence is appealing, the association between chronic energetic conditions and levels of ovarian *hormonal* function remains circumstantial. It is still possible that the empirical association between tempo of maturation and adult ovarian function is not the result of a physiological adjustment of adult function to the conditions experienced during development, but rather the consequence of a persistence of acute environmental factors through time, which delay pubertal maturation in adolescence and suppress ovarian hormonal function in adulthood.

To discriminate between this alternative hypothesis and the developmental hypothesis as postulated by Ellison (1996), namely that conditions during growth and development "set" baseline levels of ovarian hormonal function, it would be necessary to examine individuals who have experienced discontinuity in environmental conditions at different stages of the life cycle. This chapter presents such a study.

Here, a migrant study was used as a natural experiment to evaluate the effects of environmental conditions on adult levels of ovarian hormonal function, and to assess whether there are any critical windows during development when changes in such conditions may have more significant effects. The study contrasted groups of similar genetic background who, as a result of migration, spent their formative years in contrasting environments; namely Sylhet, Bangladesh (poor living standards) and London, England (higher living standards).

Bangladeshi women in the present study represent a moderate population with ecological conditions — most importantly nutrition and pathogen load — that can be characterised as intermediate between previously studied subsistence and Western populations (Ellison *et al.*, 1993b). For the Bangladeshi women alluded to here, the experience of adverse energetic conditions throughout development is more likely related to chronic immunological challenges associated with the poor and insalubrious environment in which they live, rather than to high workloads and/or chronic undernutrition as in the subsistence populations referred to above.

The hypotheses tested were:

A)   Poor conditions experienced during infancy and childhood will result in adult women having lower average baseline levels of ovarian steroid hormones (progesterone and oestradiol) than those living in more affluent conditions. Prediction A: Sylheti women and adult migrants will have lower ovarian steroids than child migrants, second-generation women and white women.

B)   A positive change in environmental conditions that impacts developmental tempo will be reflected in enhanced reproductive hormonal function; migrants who move to an affluent environment while

growth and development is ongoing, will have higher ovarian steroid levels than sedentees. Prediction B: Child migrants will have levels of ovarian steroids that are negatively correlated with pre-pubertal age at migration.

C)   Baseline levels of steroid levels established during development will not be reset by improved chronic conditions after maturation. Variation in response to short-term acute energetic conditions will affect steroid levels relative to such baseline but will not override the set points established during early life. Prediction C: Adult migrants will have baseline steroid levels that are comparable to Sylheti sedentees even if their current adult energetic conditions are dissimilar.

The alternative to the developmental explanation for the association between maturation tempo and ovarian function is that this relationship, instead of being causal, occurs as the result of the effect of acute factors that persist throughout life and that affect both (developmental tempo and ovarian function) in the same direction but in an independent and unrelated manner. Under this premise, an empirical association between age at menarche and indices of adult ovarian hormonal function might still occur but not reflect a physiological adjustment of adult function contingent on conditions during development. Thus, any discontinuity in environmental conditions at any point in the life cycle has the potential to affect chronic levels of ovarian steroids; improvements in conditions will result in higher levels of these hormones, while deterioration in conditions will result in lower levels. If this alternative hypothesis were true then, compared to Sylheti sedentees, both adult and child migrants will have high levels of adult ovarian steroids that are positively correlated with length of time spent in the UK.

Contrasting environments

The study design presupposes that the two formative scenarios (conditions in Bangladesh vs. UK) are indeed different with respect to how conducive they are for attaining a developmental tempo that results in expression of optimal genetic potential.

In the absence of first-hand longitudinal growth and health data for the participants in this study, general statistics published in the literature on childhood and maternal health, as well as on economic and health indicators for Bangladeshi, South Asian and general populations in the UK are presented in table 13. These will be used to substantiate the argument that women in all different groups in the present study are likely to have experienced considerably different environmental conditions during development depending on their country of birth and the place where they grew up.

Table 13. Health and development statistics for Bangladesh and the UK.

	BANGLADESH	UK
GNP per capita (USD)	400	28,350
Urban population (% of total population)	24	89
% of population living below poverty line	50	..
Illiteracy (% of population age 15+)	59	..
% of population with access to sanitation	31% rural, 81% urban	na
Number of physicians (per 1000)	0.2	0.6
Life expectancy for women (yrs)	62	81
Female adult mortality (per 1000)	258	67
Maternal mortality		
Lifetime risk	1 in 42	1 in 4600
Mortality ratio (per 100,000 births)	600	10
Prevalence of anaemia (non-pregnant, non-lactating women)	61-85%	
Infant mortality		
Infant mortality rate (per 1000 live births)	48	5
Infant mortality rate of under 5 (per 1000 live births)	73	7
Prevalence of anaemia (children under 5)	27-55%	..
Prevalence of different parasitic infections (children under 5)	>65%	..
Prevalence of moderate and severe wasting (children under 5)	10%	..
Prevalence of moderate and severe stunting (children under 5)	45%	..
Low Birthweight rate (<2500g)	39%	8%

As mentioned earlier in the chapter pertaining to the description of the study population, participants in Bangladesh are of middle-class ascription, live in solid dwellings with access to either tube or well water, experience no evident food insecurity and have low levels of energy expenditure. Despite the seemingly adequate conditions, Sylhet town lacks appropriate sewage and waste disposal systems, has limited water treatment capacity and is subjected to seasonal river flooding which makes it an unsanitary environment where infection and disease are rife and potable water is scarce. This insalubrious situation is exacerbated by the limited availability and poor quality of health care provisions. This substandard state of affairs for even the relatively affluent part of Sylheti society to which the participants in the study belong is confirmed by their frequent reports of infection-related childhood deaths and maternal mortality during childbirth among close relatives and friends. In this context, the data reported in Table 13 as well as the following statistics on childhood and maternal health are telling and help to substantiate the argument that Bangladeshi migrants in England experience a considerable improvement in quality of life, particularly with regard to health.

The prevalence of stunting and wasting among female children under five in Sylhet Division was 28% and 8% respectively, for girls whose mothers had completed secondary or higher education, and 18% of these mothers were themselves wasted (NIPORT, 2001). In metropolitan areas prevalence of anaemia among children under five was 27% and 61% for non-pregnant non-lactating females. The prevalence of chronic undernutrition (BMI<18) and overweight (BMI >26) among young adult females (20-24yr) in urban middle-class Bangladeshi settings was 23% and 2%, respectively. Data on calories and protein balance (required vs. intake) shows that during early childhood, females living in urban settings have a deficit of up to 42% (NIPORT, 2001).

In terms of parasitic infection, prevalences of up to 75% for different intestinal parasites have been reported for children aged 2-5 years (Northrop-Clewes *et al.*, 2001). Data on prevalence of anaemia (70%) and parasitic infection among students at Dhaka University confirm a very high prevalence (57%) of single and multiple intestinal parasitic infections even among this more affluent sector of the Bangladeshi population (Muttalib *et al.*, 1975); these conditions were possibly equivalent to those prevalent when adult migrants and sedentee women in our study were growing up. In both studies above, the commonest types of parasites found (*Ascaris lumbricoides, Entamoeba histolytica* and *Trichuris trichiura*) point to poor sanitary conditions as the main cause for transmission. The stress of such widespread exposure to infection, either chronic or recurrent, even if asymptomatic, is likely to divert resources during development even in adequately fed infants and children. The anthropometric statistics presented above are consistent with such expected growth faltering (Solomons *et al.*, 1997; Campbell *et al.*, 2003; Solomons, 2003).

Despite the fact that Bangladeshis in the UK have socio-economic indicators that reflect their socially disadvantaged position relative to the general population (see details in Chapter 2), the overall quality of the environment and the wide access to health services and a clean water supply in the UK is a radical departure from conditions in Sylhet. If nothing else, migrants to the UK are free from the chronic exposure to infections, and for children this should immediately translate into improved conditions for growth (Tanner, 1992). A study on helminth infections among Asian women attending an antenatal clinic in England found that 45% of the Bangaldeshi women were infected with at least one of three species of worms, and showed that the prevalence of infection decreased dramatically among longer residents in the UK (Constantine *et al.*, 1988).

Longitudinal data on growth patterns of children from different ethnic groups in the UK is lacking, particularly for the critical period of infancy and puberty. However, the estimates available from cross-sectional studies suggest that the growth of infants (4-40 months) and children (5-14 yrs) of South Asian background is indeed comparable to the 1990 UK growth standards (Gatrad *et al.*, 1994; Duggan & Harbottle, 1996; Kelly *et al.*, 1997; Lawson *et al.*, 1998). Data also confirm a secular trend towards increased height in succeeding generations, especially in females (Chinn *et al.*, 1996; Shams & Williams, 1997; Chinn *et al.*, 1998; Chinn & Rona, 2004). With regard to maturation, there are no comparative data on age at menarche between ethnic groups and the general population, nor on secular trends between succeeding generations of migrants in the UK. However, there is widespread evidence of earlier menarcheal ages associated with improved socio-economic and sanitary conditions both within and between populations (Tanner, 1973) that often parallel trends in increasing height (Cole, 2000). It is therefore reasonable to assume that the improved conditions in the UK compared to Sylhet, would also impact maturational tempo and translate into earlier menarche.

Regarding infant and child health, a study in East London, where the concentration of Bangladeshi immigrants is highest, revealed that post-neonatal mortality rates for infants born to Bengali mothers between 1987 and 1990 was 6.9 per thousand live births, compared with 9.4 per thousand for infants born to mothers of Anglo-European origin in the same area (Hilder, 1994); an enormous contrast to the national rates for Bangladesh of 63/1000 births (UNICEF, 2004 www.childinfo.org). This tenfold decrease in mortality rates is observed even though the prevalence of low birth weight (<2500g) among UK-born Asian infants remains high (Jivani, 1986; Collins *et al.*, 1997; Harding *et al.*, 2004); presumably related to Asian women having fewer birth complications as a result of having smaller babies.

In the same line, the latest figures from the Health Survey of Young People in the UK point that 2-15 year old girls of Bangladeshi ethnicity fare relatively better than the general population as judging by the incidence of doctor diagnosed asthma, longstanding illness, limiting long standing illness, and acute sickness (ONS, 2004b). The fact that this survey does not mention parasitic infections as a cause of concern among children and adolescents aged 0-19 years is further evidence of a more salubrious environment in the UK. An additional indirect indicator of poorer conditions abroad compared to the UK is the fact that the highest rate of cases of childhood tuberculosis among children of Asian ethnicity is found in children born outside Britain. Similarly, prevalence of hepatitis B among South Asian pregnant women is higher in those born abroad compared to that in the general British population (ONS, 2004b).

In summary, the available nutritional and health data on Bangladeshis in Sylhet and of South Asians in the UK are in line with the notion that environmental conditions experienced during growth and development by each group are indeed very different, with those enjoyed in the UK less immunologically stressful and therefore more conducive to optimum growth and maturation than those of Bangladesh.

Methods

Subjects and study protocol

The study recruited healthy women of reproductive age (18-39 years) who were not currently (or had not been for at least the past three months) pregnant, lactating, or using steroid-based contraceptives (oral, injectables, implants or steroid-releasing IUDs), with no clinical history of diabetes, thyroid disorders, infertility and/or reproductive disorders. Only women with menstrual cycles >23 days and <37 days long who reported cycle regularity (i.e. never or rarely missing a menses) were accepted into the study. These criteria aimed to screen out women whose

reproductive steroid levels would be altered by certain pathologies or exogenous hormones.

Participants were divided into five groups according to their country of birth and, in the case of first generation migrants, age at migration:

♦ Bangladeshi women living in Sylhet, Bangladesh who were born and raised there (SYL=48).

♦ First-generation Bangladeshi migrants who spent their infancy and childhood in Sylhet, Bangladesh, but moved to the UK as adolescents or adults (post-menarche) (ADU=56).

♦ First-generation Bangladeshi migrants who spent their infancy in Sylhet, Bangladesh, but moved to the UK as young children (pre-menarche) (CHI=42).

♦ Second generation Bangladeshi migrant women who were conceived, born and raised in the UK but whose parents moved from Sylhet, Bangladesh, to the UK (2ndGEN=33).

♦ Non-Bangladeshi, white women living in similar neighbourhoods to the immigrant Bangladeshis in London, whose parents and at least both grandmothers were born in the UK (WHI=48).

Based on the three phases of growth recognised in the literature of childhood development (Karlerberg *et al.*, 1994), migrants who arrived in the UK *before* menarche were also classified into three subgroups to facilitate further analyses:

a) infancy (0-2 years) (n=5);

b) childhood (3-8 years) (n=17); and

c) peri-menarche (≥9 years) (n=17).

Except for the occasional short visit to Bangladesh, all migrant women have lived in the UK uninterruptedly since migration. Similarly, Sylheti, second generation and white women have lived continuously in Bangladesh or the UK, respectively.

Participants collected daily saliva samples at home for the duration of a menstrual cycle starting on the first day of menses, and recorded the following information in a calendar: start of menses, days of menstrual bleeding, and start of the subsequent cycle. Participants were encouraged to collect the samples at roughly the same time of the day. At the end of collection, anthropometric measurements (height, weight, and skinfolds) were taken following standard procedures (Gibson, 1990) (see Appendix C) and two questionnaires (general sociodemographic and food-frequency) were administered by a bilingual female research assistant (see Appendix A & B for originals). For detailed questionnaire results and discussion refer to Chapter 2.

Saliva sample collection, handling and storage

Samples consisted of 5 ml of saliva collected in polystyrene tubes pre-treated with sodium azide as a preservative to a final concentration of approximately 0.1%. Women were given a sugarless spearmint flavoured gum as salivary stimulant. This gum has been extensively tested and does not interfere with analyses of salivary progesterone and oestradiol (Ellison, 1988; Lu *et al.*, 1997). Following the results of the pilot study (Chapter 4), women were requested to refrain from chewing betel nut, and eating or brushing their teeth (in case of bleeding gums which might contaminate the saliva sample) for a minimum of one hour prior to sample collection.

Samples were kept at ambient temperature until retrieved and shipped to the laboratory at Northwestern University, Chicago where they were kept at −20°C until assayed. Samples from all groups had comparable collection, handling, storage and assay conditions. Previous work has demonstrated that salivary steroids are stable for extended periods and that treating samples prior to collection with sodium azide allows storage at ambient temperatures for up to six months without statistically significant distortion of results due to degradation (Ellison, 1988; Lipson & Ellison, 1989a). Saliva samples were assayed for progesterone and

oestradiol using standardised radioimmunoassay techniques described previously (Lu *et al.*, 1997, 1999), and detailed in Appendix D. All samples from a given individual were run in the same assay to minimise the effects of interassay variability. Cycles from all five different study groups were included in each assay, again to minimise the impact of inter-assay variability on potential group differences. Approximately 10 cycles were run per assay, yielding a total of 27 assays for each hormone. The intra-assay coefficient variation (CV) calculated from the differences of duplicate determinations of samples averaged 14.6% for oestradiol and 11.6% for progesterone. Interassay CVs from quality control (QC) pools averaged 19.9% for oestradiol and 14.7% for progesterone. The sensitivity limit of the assay was 31 pg/ml for progesterone and 1.56 pg/ml for oestradiol.

Hormone data analysis

Saliva, unlike plasma or urine, is an easy, non-invasive and non-disruptive way to measure hormone levels. Salivary assays yield results that directly reflect the free, biologically active steroid concentration in blood (Ellison, 1988). Salivary progesterone and oestradiol profiles have been readily used to categorise individual menstrual cycles and as indicators of ovarian function (Ellison, 1988; O'Rourke & Ellison, 1988; Panter-Brick *et al.*, 1993; Lipson & Ellison, 1996; Lu *et al.*, 1999; Vitzthum *et al.*, 2002).

Ascribing ovulation

Ascription of ovulation has been conducted by a number of methods, the most commonly used being an algorithm that discriminates ovulatory from anovulatory cycles by examining luteal phase activity, defined operationally by a progesterone value greater, or equal to, two standard deviations from mean follicular levels in the same cycle from an individual (Ellison, 1988; Lipson & Ellison, 1996). In the present study, this algorithm cannot be applied since progesterone was only assayed

for the last 18 samples of the cycle and, therefore, values for the follicular phase are incomplete. However, unlike many of other studies that have used the above algorithm, this study does have oestradiol profiles across the entire cycle which can be used to complement the progesterone data, and to assess whether a cycle is ovulatory or not. The juxtaposition of the two steroids in the same profile permits the inspection of hormonal patterns associated with ovulation (an oestradiol peak at mid-cycle followed by a luteal rise in progesterone) to estimate ovulation day (O'Rourke & Ellison, 1988).

In this study, while progesterone profiles were derived from the luteal phase only as discussed above, oestradiol was analysed over the entire menstrual cycle. Both hormones were plotted in a single profile against cycle day, and the day of ovulation was estimated as the first or second day (that with the lowest oestradiol value) after the mid-cycle peak of salivary oestradiol. This point was meant to coincide with the beginning of a luteal progesterone rise, although in some cases this rise was slightly delayed. Those cycles that complied with these characteristics were assumed to be ovulatory (Lipson & Ellison, 1996). Ovulation day as determined by visual inspection was set as Day 0, and all individual profiles re-aligned accordingly. The follicular phase was taken to comprise days -14 to −1 and the luteal phase days 1 to 14. In order to standardise cycle length for analysis, those cycles longer than 29 days were trimmed at the beginning (mostly coinciding with the days of menstrual bleeding). Those cycles where critical sections of the profile (i.e., mid-cycle where ovulation was expected) were missing due to incomplete sampling were not included in the analysis. Neither were those where the luteal rise was absent. Out of a total 227 cycles, ovulation was not discernible in only 17 cases.

Progesterone and oestradiol indices

Two variables for progesterone and 4 for oestradiol, as indicated below, were calculated for each cycle as quantitative indices of ovarian function

to be used in statistical analysis (Figure 5). Data from individual women were pooled within study groups and averages per group calculated. All data are presented in pg/ml.

Progesterone (P) indices:

Mean luteal P: estimates mean progesterone during the final 14 days of the cycle. This was calculated as the grand mean of daily mean progesterone of all women who contributed a sample on a given day for days 1 to 14.

Mean highest P luteal value: refers to the single highest observed progesterone value from days 1 to 14. This was calculated as the grand mean of the highest observed progesterone value of all women who contributed a sample for days 1 to 14.

Oestradiol (E_2) indices:

Total E_2: estimates mean oestradiol during the entire menstrual cycle. This was calculated as the average mean of daily mean oestradiol of all women who contributed a sample on a given day for days -14 to 14. This value should not to be confounded with total oestradiol meaning the sum of free and bound steroid in plasma.

Mean luteal E_2: estimates mean oestradiol during the final 14 days of the cycle. This was calculated as the average mean of daily mean oestradiol of all women who contributed a sample on a given day for days 1 to 14.

Mean follicular E_2: estimates mean oestradiol during the first 14 days of the cycle, calculated as the average of daily mean oestradiol of all women who contributed a sample on a given day for days -14 to -1.

Mean mid-cycle E_2 peak: estimates mean oestradiol during the time span -4 to 0. This was calculated as the grand mean of daily mean oestradiol of all women who contributed a sample on a given day for days -4 to 0. The chosen span represents the interval during which the pre-ovulation oestradiol peak is expected to have occurred.

Figure 5. Diagram of the menstrual cycle to illustrate how the progesterone and oestradiol indices were calculated.
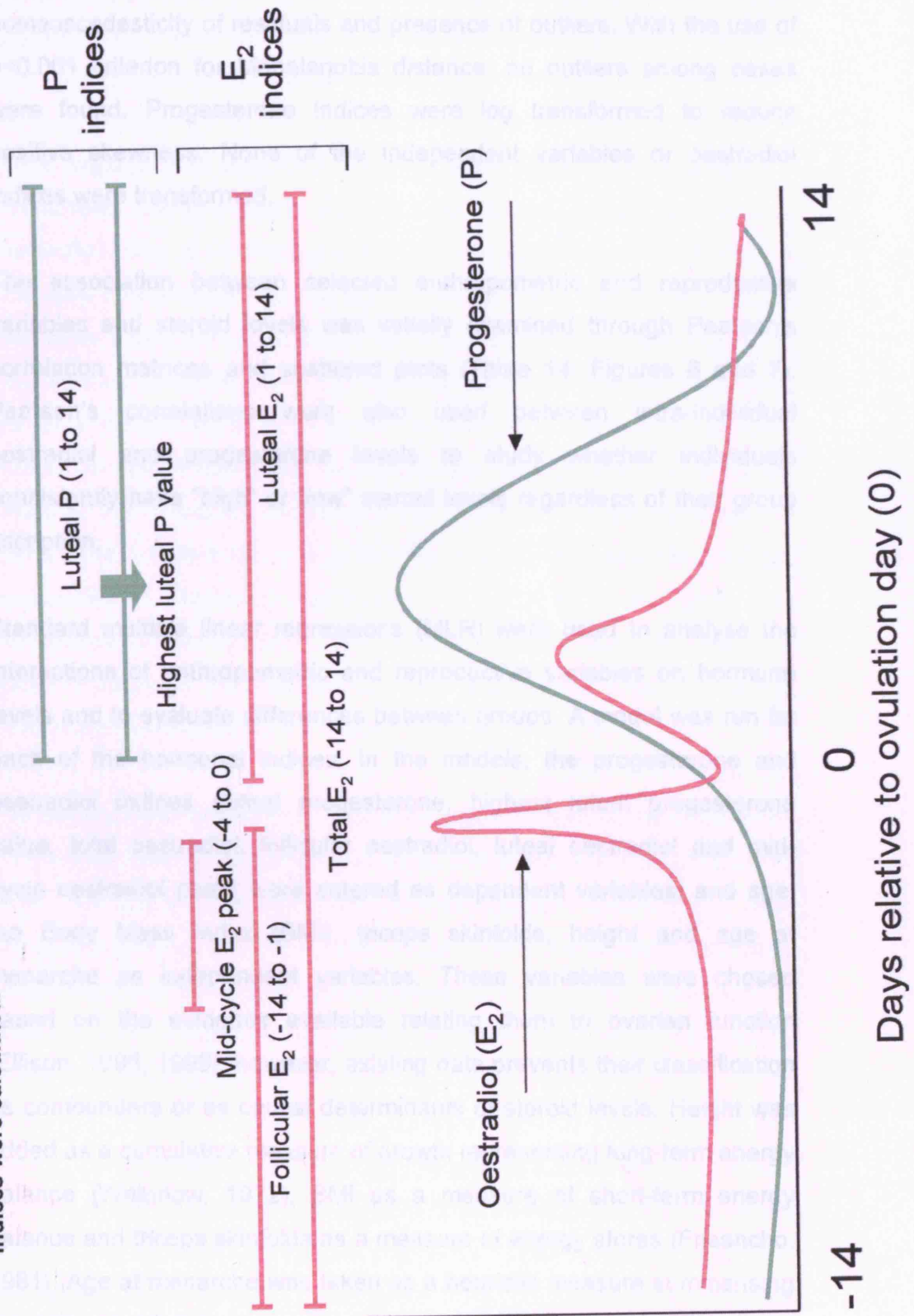
Statistical Analysis

Raw hormonal data were tested for assumptions of normality, linearity, homeoscedasticity of residuals and presence of outliers. With the use of $p < 0.001$ criterion for Mahalanobis distance, no outliers among cases were found. Progesterone indices were log transformed to reduce positive skewness. None of the independent variables or oestradiol indices were transformed.

The association between selected anthropometric and reproductive variables and steroid levels was initially examined through Pearson's correlation matrices and scattered plots (Table 14: Figures 6 and 7). Pearson's correlations were also used between intra-individual oestradiol and progesterone levels to study whether individuals consistently have "high" or "low" steroid levels regardless of their group ascription.

Standard multiple linear regressions (MLR) were used to analyse the interactions of anthropometric and reproductive variables on hormone levels and to evaluate differences between groups. A model was run for each of the hormonal indices. In the models, the progesterone and oestradiol indices (luteal progesterone, highest luteal progesterone value, total oestradiol, follicular oestradiol, luteal oestradiol and mid-cycle oestradiol peak) were entered as dependent variables, and age, the Body Mass Index (BMI), triceps skinfolds, height and age at menarche as independent variables. These variables were chosen based on the evidence available relating them to ovarian function (Ellison, 1995, 1999); however, existing data prevents their classification as confounders or as causal determinants of steroid levels. Height was added as a cumulative measure of growth representing long-term energy balance (Waterlow, 1972), BMI as a measure of short-term energy balance and triceps skinfolds as a measure of energy stores (Frisancho, 1981). Age at menarche was taken as a heuristic measure summarising the inter-correlations among various aspects of the developmental

process (Ellison, 1981c, a). To evaluate differences in hormonal levels between groups, the categorical variable "group" was entered in the model as a dummy variable, using Sylhetis as the reference group. Sample sizes varied from model to model depending on the available data for each covariate for each individual.

Visual inspection of correlation plots between steroid indices and each independent variable (age, BMI, triceps skinfold, height and age at menarche) showed no evidence of non-linear associations (Figs. 6 & 7). This was corroborated statistically by the fact that the addition of the covariates (age, BMI, triceps skinfold, height and age at menarche) in the model as quadratic terms had no significant effect on the outcome of the MLR models (data not shown), and therefore all covariates were entered in the final model as continuous and simple linear terms. Although the effect of anthropometric and reproductive variables on salivary reproductive steroids is well-documented (Ellison, 1995, 1999), the available evidence precludes any attempt to establish any precedence of one variable over another in explaining inter-individual hormone variation. For this reason, covariates were not entered in the MLR models in any deliberate order.

The independent contribution of each covariate to inter-group differences in hormonal indices was evaluated using unviariate analyses (Tables 15 & 16). To this end, women were divided into low, medium and high percentile groups (<33rd, 34-66th, and >67th percentile) for each independent variable (age, BMI, triceps skinfold, height and age at menarche) and entered in the general linear model, along with "group", as independent categorical factors.

Central to the present study's working hypotheses is the ability to divide individuals into categories according to their developmental stage when exposed to new environmental conditions upon arrival in the UK. Menarcheal status (pre- vs. post-menarcheal) at the time of migration

was chosen as the classification criterion because of its value as a heuristic indicator of other growth and developmental landmarks (skeletal and neuro-endocrinological) (Ellison, 1981c, a). This landmark event implies a shift in resource allocation priorities from growth to reproduction, and presumably a change in susceptibility to discontinuous resource availability and, by implication, in the potential to affect ovarian function. First generation migrant women were therefore classified as "adult" and "child" migrants according to whether they had reached menarche or not at the time of entry into the UK.

This approach is suitable for testing the working hypotheses regarding differences in ovarian function and in proxies of developmental tempo among study groups. However, the approach is inappropriate to test one of the predictions derived from hypothesis B concerning the correlation between levels of ovarian function and age at migration. Specifically, the use of menarcheal status at the time of migration to define the child migrant group inherently generates a spurious positive association between age at migration and age at menarche, in particular among women who arrived in the UK within the range for menarcheal age exhibited by participants in this study (9-16 years). As age at menarche is known to be inversely related to levels of adult reproductive steroids, this limitation is also relevant for estimates regarding the relationship between age at migration and steroid levels.

In an attempt to surmount this problem, first generation women were classified according to whether their age on arrival was younger or older than the maximum recorded age at menarche for all first generation (Bangladesh-born) migrants in the study (i.e. 16 years). The rationale being that by age 16, all women in this sample would have reached menarche regardless of their location. Thus, women who arrived in the UK aged ≤16 years were classified as "child" migrants, whereas those who entered the country at older ages (>16 years) were categorised as "adults", *irrespective* of their real (self-reported) menarcheal status at

time of entry. Figure 8 shows the distribution of actual menarcheal age in relation to age at entry into the UK.

This conservative classification was adopted for the Pearson's correlation analyses used to examine the effect of age on arrival to the UK on age at menarche, steroid levels and height; as well as in the assessment by the same method, of the effect of the length of exposure (time spent in the UK) on steroid levels among women who migrated after puberty.

Another approach used to evaluate the effect of the timing of changes in environmental conditions on ovarian function was to take only those women who migrated *before* the shift in resource allocation (actual menarche), and categorise them according to the stage of development they had reached when entering the UK, namely: infancy (0-2 years), childhood (3-8 years) and peri-menarche (>9 years). These categories roughly coincide with stages of neuro-endocrine development related to growth and maturation and, thus, may be relevant to the development of ovarian function (Karlerberg *et al.*, 1994). One-way ANOVAs were used to compare these three developmental categories with respect to adult steroid levels (progesterone and oestradiol indices), growth (final stature) and maturation (age at menarche).

Standard multiple linear regressions (MLR) were used to examine differences in BMI and triceps skinfolds between groups relative to Sylhet sedentees. A model was run for each anthropometric measurement adjusted by age, parity and group. Group differences in age at menarche were examined by ANOVA and were Bonferroni adjusted.

The results of the pilot study described in Chapter 4 showed that the distorting effects of betel nut chewing on the measurement of salivary steroids by radioimmunoassay techniques are transitory. Here a two-way

ANOVA was used to assess whether betel nut chewing has any detectable long-term effect on adult salivary progesterone and oestradiol levels that could act as a confounding factor when comparing hormonal levels among chewers and non-chewers in a population that practices betel nut chewing, as well as when comparing women in a population that consume betel nut versus one that does not. All sedentees, first- and second generation Bangladeshi participants were classified into either betel nut chewers or non-chewers according to the information provided in the general questionnaires. Comparisons of luteal progesterone and total oestradiol indices between betel nut chewers and non- chewers were compared by two-way ANOVA and controlled for group.

Statistical analyses were performed using SPSS v. 10.0 for the Macintosh. The significance level was set at $p < 0.05$.

Table 14. Bivariate and partial correlation matrices between hormone indices, age, age at menarche and anthropometrics (all 5 groups).

	LUTEAL PROGESTERONE	TOTAL OESTRADIOL	AGE	BMI	TRICEPS	HEIGHT	LUTEAL PROGESTERONE
							Partial correlations controlling for group
TOTAL OESTRADIOL							
Pearson Correlation	-0.12	..	..	..	..	..	-0.09
Sig. (2-tailed)	0.13	..	..	..	..	..	0.24
N	175	..	..	..	..	..	164
AGE							
Pearson Correlation	-0.10	0.05	..	..	..	..	-0.15
Sig. (2-tailed)	0.15	0.49	..	..	..	..	0.04 *
N	198	194	..	..	..	..	164
BMI							
Pearson Correlation	-0.23	0.09	0.33	..	..	..	-0.21
Sig. (2-tailed)	0.00 **	0.22	0.00 **	..	..	..	0.01 **
N	196	192	214	..	..	..	164
TRICEPS							
Pearson Correlation	-0.16	0.03	0.28	0.76	..	..	-0.18
Sig. (2-tailed)	0.03 *	0.73	0.00 **	0.00 **	..	..	0.02 *
N	192	189	211	210	..	..	164
HEIGHT							
Pearson Correlation	0.20	-0.11	0.00	-0.16	-0.04	..	0.05
Sig. (2-tailed)	0.00 **	0.13	0.98	0.02 *	0.61	..	0.56
N	196	193	215	214	211	..	164
MENARCHE							
Pearson Correlation	-0.17	0.03	0.14	-0.09	-0.11	0.15	-0.17
Sig. (2-tailed)	0.02 *	0.68	0.05	0.21	0.11	0.03 *	0.03 *
N	192	190	211	209	207	210	164

*p<0.05; **p<0.01

Figure 6. Correlation plots for luteal progesterone index and age, age at menarche and anthropometric variables (all 5 groups).
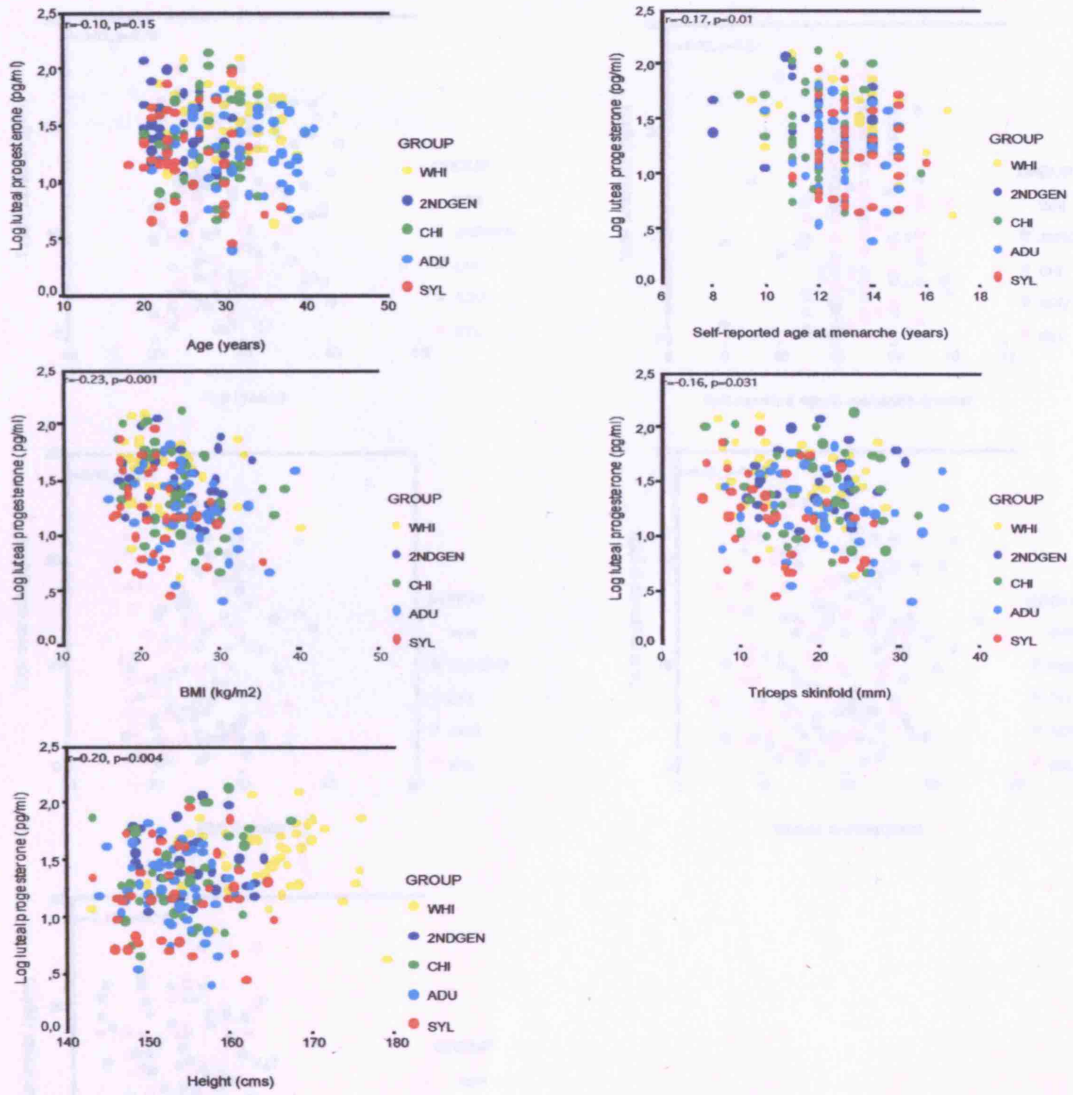
Figure 7. Correlation plots for total oestradiol index and age, age at menarche and anthropometric variables (all 5 groups).

Results
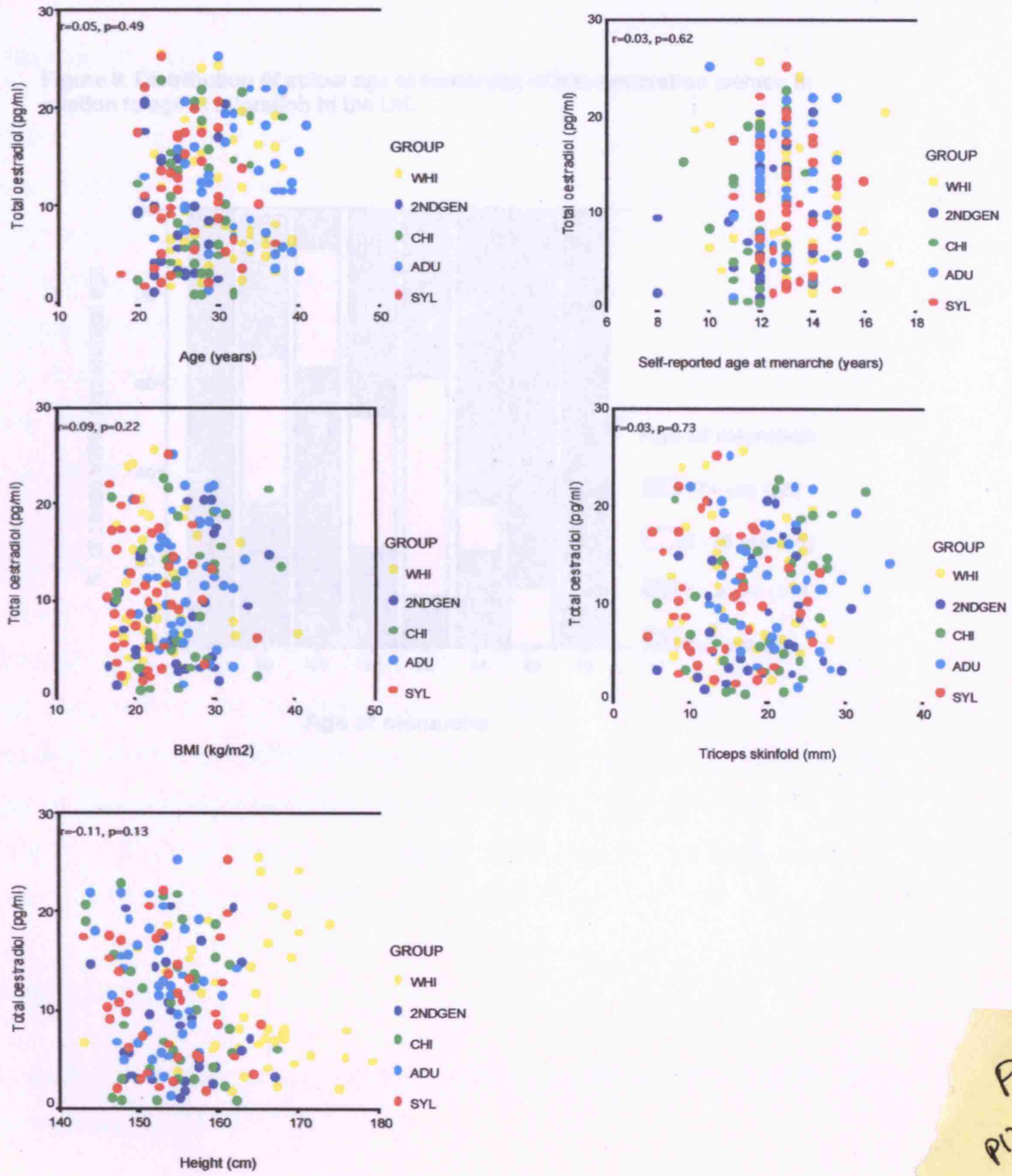
Figure 8. Distribution of actual age at menarche of first-generation women in relation to age at migration to the UK.

Figure showing a stacked bar chart. Y-axis: "% of cases within menarcheal age" from 0 to 100. X-axis: "Age at menarche" from 9 to 16.

Legend — Age at migration:
- 17+ yrs (38)
- 9 -16 yrs (28)
- 3 - 8 yrs (17)
- 0 -2 yrs (5)

Results

There was no significant correlation between intra-individual oestradiol and progesterone levels (r = -0.12, p = 0.10, n = 175) suggesting that "high/low" individuals do not exist within the study population. Saliva samples were collected over a period of several months spanning a couple of seasons, but, preliminary analysis confirmed there was no significant effect of season of collection on average steroid levels (one-way ANOVA $F_{3,183}$ = 1.35, p = 0.25 for progesterone; $F_{3,181}$ = 1.05, p = 0.37 for oestradiol).

Betel nut chewers and non-chewers did not differ significantly with regard to luteal progesterone and total oestradiol indices, even after controlling for group, which suggests that the practice of chewing betel nut does not have a long-term effect on levels of salivary reproductive steroids. (two-way ANOVA $F_{7,138}$ = 1.67, p = 0.12; group p=0.03; betel nut yes/no p=0.95; group*betel yes/no p=0.95 for progesterone; $F_{7,138}$ = 0.88, p = 0.52; group p = 0.33; betel nut yes/no p = 0.77; group*betel yes/no p = 0.89 for oestradiol).

Anthropometrics

Descriptive statistics of anthropometric variables by group are summarised in Table 17.

Height

One-way ANOVA showed significant differences in height between groups ($F_{4,244}$ = 36.82, p = 0.001). White women were significantly taller (163.9 ± 1.0 cm) than women in all other groups ($\bar{x}$ = 153.2 ± 0.8 cm for Sylheti sedentees; $\bar{x}$ = 152.5 ± 0.3 cm for adults; $\bar{x}$ = 154.2 ± 0.7 cm for child migrants; $\bar{x}$ = 155.2 ± 0.9 cm for second generation women) (Table 17).

Among first generation women who arrived earlier than the upper limit of the age at menarche range for their group ($\leq$ 16 years) (child migrants), the negative correlation between height and age at migration fell short of significance (r = -0.25, p = 0.07). However, ANOVA shows that women who arrived in early infancy (aged 0-2) are significantly taller ($\bar{x}$ = 159.8 $\pm$ 1.8 cm) than those who migrated at later ages ($\bar{x}$ = 154.0 $\pm$ 1.0 cm for arrivals at 3-8 years old; $\bar{x}$ = 152.8 $\pm$ 1.0 cm for arrivals aged $\geq$9 years) ($F_{2,50}$= 4.72, p = 0.01).

BMI and triceps skinfolds

General linear models show significant differences in BMI and triceps skinfolds between groups and unlike parity, age has a significant positive effect (BMI: age $F_{1,213}$ = 9.7 p = 0.002; group $F_{4,123}$ = 4.4 p = 0.01; parity $F_{1,213}$ = 3.4 p = 0.11; group*parity $F_{4,213}$ = 2.3 p=0.37; triceps skinfolds (age $F_{1,239}$ = 5.0 p = 0.02; group $F_{4,239}$ = 2.7 p = 0.03; parity $F_{1,239}$ = 1.17 p = 0.27; group*parity $F_{4,238}$ = 0.71 p=0.58) (Table 17). Multiple linear regression models indicate that after correcting for these factors, first- and second generation migrants' mean BMI and triceps skinfolds are significantly higher than those of Sylheti sedentees. White women do not differ from their Sylheti counterparts in this respect (Table 18).

Relationship between anthropometric, reproductive and endocrine variables.

Table 14 shows the correlation and partial correlation (controlled for group) matrices for the association between each of the independent variables (age, height, BMI, triceps skinfold, age at menarche) and luteal progesterone and total oestradiol indices for all study groups. These relationships are depicted graphically in figures 6 & 7.

Measures of short-term and current energy balance (BMI and triceps skinfold respectively) showed a significant negative correlation with mean luteal progesterone, which remained after controlling for group (r = -0.21 for BMI; r = -0.18 for triceps skinfold). The negative associations

between age at menarche and luteal progesterone (r = -0.17), and age and this steroid index (r = -0.15) were also significant after controlling for group, whereas the positive correlation between height and this hormonal index was not (Table 14). None of the correlations between the independent variables and total oestradiol were significant. The positive association between age at menarche and height was also significant even after controlling for group (r = 0.20).

A summary of mean progesterone and oestradiol indices by group *before* adjustment for independent variables (age, age at menarche, BMI, triceps skinfolds and height) is presented in table (Table 19). Raw *unadjusted* mean luteal progesterone levels and highest luteal progesterone values in Sylheti women were significantly lower than those in child migrants, second generation and white women but indistinguishable from those of adult migrants (Table 19). In contrast, no significant group differences were found for any of the raw unadjusted oestradiol indices. When corrected for each independent variable separately in univariate models, BMI and triceps skinfolds (as categorical variables) showed a significant effect on the luteal progesterone index (Table 15), but contrasts between groups remained the same as in the unadjusted comparisons above. When all covariates were entered simultaneously in a multiple linear regression model, the individual contributions of the independent variables to differences in luteal progesterone index among groups were no longer significant but the pattern of such differences between groups was maintained (Tables 20 & 21).

None of the covariates had a significant effect on mean total oestradiol levels, either individually or simultaneously in univariate or multivariate models respectively (Tables 16, 22 & 23).

Age at menarche

One-way ANOVA showed significant differences in self-reported age at menarche between groups ($F_{4,210}$ = 5.3, p=0.001) (Table 17). Child migrants (defined as women entering the UK aged <=16) reached menarche at an earlier age ($\overline{X}$ = 12.2 ± 0.2 yr) than either Sylheti sedentees ($\overline{X}$ = 13.2 ± 0.2 yr), adult migrants (defined as entering the UK aged 17+) ($\overline{X}$ = 13.0 ± 0.2 yr), or white women ($\overline{X}$ = 13.1 ± 0.2 yr) but at similar ages than second generation women ($\overline{X}$ = 12.3 ± 0.3 yr), who had an earlier menarche than women in Sylhet.

With regard to the effect of age at migration on menarcheal age among all first generation women, results show a significant positive correlation: younger arrivals attain menarche earlier (r = 0.35, p = 0.001). When these women are divided into child and adult migrants using the ≤ 16 / 17+ years at migration criteria, the positive correlation is still significant for the child migrant group (r = 0.31, p = 0.03) but not for the adults (r = - 0.07, p = 0.65, n = 40) (Figure 9).

Women who migrated to the UK during the childhood phase show significantly earlier age at menarche ($\overline{X}$ = 11.9 ± 0.3 yr) than later first generation arrivals ($\overline{X}$ = 12.4 ± 0.2 yr and $\overline{X}$ = 13.0 ± 0.5 yr for peri-menarche and post-menarche, respectively) ($F_{3,89}$ = 3.98, p = 0.01).

Table 15. Univariate general lineal models for luteal progesterone index (log) as dependent variable [a]

Model	F (df)	Adj. R²	p
GROUP	$F_{4,196}=8.17$	0,13	$p = 0.00$ **
AGE	$F_{2,196}=0.99$	0,17	$p = 0.37$ ns
GROUP	$F_{4,196}=7.77$		$p = 0.00$ **
AGE*GROUP	$F_{7,196}=0.54$		$p = 0.79$ ns
BMI	$F_{2,196}=7.75$	0,17	$p = 0.02$ *
GROUP	$F_{4,196}=7.61$		$p = 0.00$ **
BMI*GROUP	$F_{8,196}=1.18$		$p = 0.31$ ns
TRICEPS	$F_{2,192}=2.34$	0,14	$p = 0.00$ **
GROUP	$F_{4,192}=7.20$		$p = 0.00$ **
TRICEPS*GROUP	$F_{8,192}=0.14$		$p = 0.90$ ns
HEIGHT	$F_{2,196}=1.18$	0,13	$p = 0.31$ ns
GROUP	$F_{4,196}=4.50$		$p = 0.00$ **
HEIGHT*GROUP	$F_{8,196}=1.21$		$p = 0.29$ ns
AGE AT MENARCHE	$F_{2,192}=1.16$	0,18	$p = 0.31$ ns
GROUP	$F_{4,192}=7.44$		$p = 0.00$ **
AGE AT MENARCHE*GROUP	$F_{8,192}=0.80$		$p = 0.80$ ns

*p<0.05; **p<0.01

All independent factors (age, BMI, triceps, height and age at menarche) were entered as categorical variables; each divided into three percentile groups (low, medium, high).

[a] Luteal progesterone index as dependent variable and group and each of the anthropometric and reproductive variables separately as independent factors.

Table 16. Univariate general lineal models for total oestradiol index as dependent variable [a]

Model	F (df)	Adj. R [2]	p
GROUP	$F_{4,194}=1.41$	0,23	p = 0.00 **
AGE	$F_{2,194}=0.31$	-0,01	p = 0.72 ns
GROUP	$F_{4,194}=1.00$		p = 0.40 ns
AGE*GROUP	$F_{7,194}=0.66$		p = 0.69 ns
BMI	$F_{2,192}=0.80$	-0,02	p = 0.45 ns
GROUP	$F_{4,192}=1.63$		p = 0.17 ns
BMI*GROUP	$F_{8,192}=0.27$		p = 0.97 ns
TRICEPS	$F_{2,189}=1.44$	-0,02	p = 0.23 ns
GROUP	$F_{4,189}=1.82$		p = 0.12 ns
TRICEPS*GROUP	$F_{8,189}=0.29$		p = 0.96 ns
HEIGHT	$F_{2,193}=0.59$	-0,03	p = 0.94 ns
GROUP	$F_{4,193}=0.06$		p = 0.33 ns
HEIGHT*GROUP	$F_{8,193}=0.28$		p = 0.97 ns
AGE AT MENARCHE	$F_{2,190}=1.21$	0,01	p = 0.29 ns
GROUP	$F_{4,190}=1.21$		p = 0.34 ns
AGE AT MENARCHE*GROUP	$F_{8,190}=1.12$		p = 0.34 ns

*p<0.05; **p<0.01

All independent factors (age, BMI, triceps, height and age at menarche) were entered as categorical variables; each divided into three percentile groups (low, medium, high).

[a] Total oestradiol index as dependent variable and group and each of the anthropometric and reproductive variables separately as independent factors.

Table 17. Summary of mean unadjusted age, age at menarche and anthropometrics by group.

	SYL	ADU	CHI	2NDGEN	WHI
Age (yrs) [a]					
mean	26.1	31.8	27.8	24.4	31.2
SE	0.6	0.7	0.6	0.6	0.7
n	52	62	50	34	50
Age at menarche (yrs) [b]					
mean	13.2	13.0	12.2	12.3	13.1
SE	0.2	0.2	0.2	0.3	0.2
n	44	40	50	31	46
Height (cm) [c]					
mean	153.2	152.5	154.2	155.2	163.9
SE	0.8	0.5	0.7	0.9	1.0
n	52	61	51	34	50
BMI (kg/m2) [a] [d]					
mean	22.6	26.4	25.6	25.1	23.4
SE	0.6	0.5	0.7	0.9	0.7
n	52	61	51	34	49
Triceps (mm) [a] [e]					
mean	15.6	20.4	19.7	18.9	17.3
SE	0.9	0.8	0.9	1.2	0.9
n	52	60	50	34	46

BMI (kg/m^2) by age (X ± SE; n)

	SYL	ADU	CHI	2NDGEN	WHI
18-25 y	21.8 ± 0.8 (28)	22.5 ± 1.2 (9)	24.2 ± 1.5 (16)	25.2 ± 1.1 (23)	21.2 ± 1.0 (8)
26-30 y	21.3 ± 0.8 (14)	25.2 ± 0.8 (16)	26.5 ± 1.1 (18)	24.5 ± 1.6 (10)	22.0 ± 1.1 (13)
31-35 y	25.0 ± 1.4 (8)	27.5 ± 1.1 (16)	25.5 ± 1.3 (15)	26.8 ± 0.0 (1)	22.9 ± 1.1 (15)
36-39 y	33.4 ± 2.1 (2)	28.3 ± 0.8 (20)	31.5 ± 0.0 (1)	..	26.5 ± 1.8 (13)

BMI (kg/m^2) ** (% prevalence within group)

Parous women	(n=13)	(n=53)	(n=28)	(n=10)	(n=18)
BMI ≤ 20	18	..	6	..	50
21 <BMI >25	45	35	33	25	40
26 <BMI >30	27	40	28	62	..
BMI ≥30	9	25	33	12	10
Non-parous women	(n=39)	(n=8)	(n=23)	(n=25)	(n=32)
BMI ≤ 20	48	75	25	28	27
21 <BMI >25	44	25	50	28	46
26 <BMI >30	7	..	8	17	15
BMI ≥30	..	..	17	28	11

* Average values before correcting for age and parity.

** Values before correcting for age.

[a] Average values are within the 25 (SYL) and 50 percentiles (ADU, CHI, 2ndGEN, WHI) for US white persons of same group age according to the NHANES I survey. Frisancho, 1981 in (Gibson, 1990)

[b] Average values are within the 50 (SYL) and 75 percentiles (ADU, CHI, 2ndGEN, WHI) for US white persons of same group age according to the NHANES I survey. Frisancho, 1981 in (Gibson, 1990)

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] AGE: One-way ANOVA $F_{4,244}$=22.02 p<0.01; SYL<ADU, WHI p<0.01; CHI<ADU, WHI p<0.01, > 2ndGEN p<0.05; 2ndGEN<ADU, WHI p<0.01

[b] MENARCHE (CRITERIA <= 16 y (CHI) / 17+ (ADU)): One-way ANOVA $F_{4,210}$=5.3 p<0.001; SYL>CHI p<0.001, > 2ndGEN p<0.05; ADU>CHI p=0.05; WHI>CHI p<0.01

[c] HEIGHT: One-way ANOVA $F_{4,244}$=36.82 p<0.001; WHI >all groups p<0.001

[d] BMI: GLM $F_{10,213}$=6.6 p<0.01; age $F_{1,213}$=9.7 p<0.01; group $F_{4,123}$=4.4 p<0.01; parity $F_{1,213}$=3.4 ns; group*parity F4,213=2.3 ns

[e] TRICEPS: GLM $F_{10,239}$=3.26 p<0.001; age $F_{1,239}$=5.0 p<0.05; group $F_{4,239}$=2.7 p<0.05; parity $F_{1,239}$=1.17 ns; group*parity F4,238=0.71 ns

Table 18. Multiple linear regression showing determinants of BMI and triceps skinfolds

Predictors	BMI		TRICEPS SKINFOLD	
	Std. Coef. (beta)			
	Unadjusted		Unadjusted	
Age	..	0.30 **	..	0.21 *
Parity	..	0.10	..	0.10
Group (SYL as reference)				
ADU	0.4 **	0.18 *	0.39 **	0.21 *
CHI	0.27 **	0.20 **	0.30 **	0.23 **
2ndGEN	0.23 **	0.26 **	0.22 **	0.24 **
WHI	0.09 **	-0.02	0,15	0.06
Adj. R2	0,11	0,13	0,09	0,19
N	213	209	210	212
ANOVA	$F_{4,213}$= 7.44, p<0.001		$F_{4,200}$= 6.33, p<0.001	

*p<0.05; **p<0.01

Table 19. Summary of mean unadjusted hormonal indices by group.

	SYL	*ADU*	*CHI*	*2NDGEN*	*WHI*
Luteal progesterone (pg/ml) [*]					
mean	**22.2**	**24.6**	**38.9**	**40.2**	**45.1**
SE	3.1	2.5	5.7	5.5	4.3
n	39	46	39	29	45
Highest luteal progesterone (pg/ml) [b]					
mean	**80.0**	**92.0**	**105.4**	**119.1**	**137.9**
SE	7.1	7.2	9.9	11.3	1.2
n	39	46	38	29	45
Total oestradiol (pg/ml) [c]					
mean	**11.0**	**12.4**	**10.4**	**8.9**	**10.9**
SE	0.9	0.9	1.2	1.1	1.0
n	41	42	35	31	45
Follicular oestradiol (pg/ml) [d]					
mean	**10.7**	**12.3**	**10.0**	**8.7**	**10.8**
SE	1.0	1.0	1.2	1.1	1.0
n	41	42	35	31	44
Mid-cycle peak oestradiol (pg/ml) [e]					
mean	**13.9**	**14.0**	**12.5**	**10.5**	**13.1**
SE	1.1	1.1	1.4	1.3	1.2
n	41	42	35	31	44
Luteal oestradiol (pg/ml) [f]					
mean	**11.2**	**12.5**	**10.7**	**9.0**	**11.1**
SE	1.1	1.0	1.3	1.2	1.1
n	41	42	35	31	44

* Raw average values before adjusting for age, age at menarche and anthropometric variables.

[a] LUTEAL P INDEX: ANOVA $F_{4,198}=9.17$ p<0.001; SYL<CHI p<0.05, 2ndGEN p<0.01, WHI p<0.001

[b] HIGHEST LUTEAL P INDEX: ANOVA $F_{4,196}=5.71$ p<0.001; SYL< 2ndGEN p<0.05, WHI p<0.001

[c] TOTAL OESTRADIOL INDEX: ANOVA $F_{4,193}=1.41$ p>0.05

[d] FOLLICULAR OESTRADIOL INDEX: ANOVA $F_{4,192}=1.42$ p>0.05

[e] MID-CYCLE OESTRADIOL PEAK INDEX: ANOVA $F_{4,192}=1.20$ p>0.05

[f] LUTEAL OESTRADIOL INDEX: ANOVA $F_{4,192}=1.16$ p>0.05

Table 20. Multiple linear regression matrix showing determinants of luteal progesterone index

N	197	197	195	191	195	191	187
Adj. R2	0.13	0.14	0.17	0.15	0.12	0.14	0.16

Std. Coef. (beta)

Age	..	-0.17 *	..	..	..	..	-0.06 ns
BMI	..	..	-0.23 **	..	..	..	-0.16 ns
Triceps	..	..	..	-0.19 **	..	..	-0.07 ns
Height	..	..	..	..	0.04 ns	..	0.06 ns
Age at menarche	..	..	..	..	..	-0.14 *	-0.14 ns

Group (SYL as reference)

ADU	0.10 ns	0.18 ns	0.17 ns	0.15 ns	0.09 ns	0.04 ns	0.16 ns
CHI	0.25 **	0.28 **	0.31 **	0.31 **	0.25 **	0.19 **	0.26 **
2ndGEN	0.30 **	0.28 **	0.35 **	0.34 **	0.30 **	0.24 **	0.29 **
WHI	0.42 **	0.48 **	0.44 **	0.42 **	0.40 **	0.39 **	0.39 **

$*p<0.05$; $**p<0.01$

Table 21. Linear regression model for luteal progesterone Index

	Unstardised coefficient (B)	SE of B	Standardised coeficient (beta)	t value	p
Constant	1.69	0.73	..	2.31	0.02
Age	-0.00	0.01	-0.06	-0.77	0.44
BMI (kg/m²)	-0.01	0.01	-0.16	-1.51	0.13
Triceps (mm)	-0.00	0.01	-0.07	-0.66	0.51
Height (cm)	0.00	0.00	0.06	0.62	0.54
Age at menarche (yrs)	-0.03	0.02	-0.14	-1.87	0.06
Groups					
ADU	0.13	0.08	0.16	1.63	0.11
CHI	0.23	0.08	0.26	2.89	**0.00**
2ndGEN	0.29	0.09	0.29	3.33	**0.00**
WHI	0.33	0.09	0.39	3.54	**0.00**

Notes: dummy SYL as reference group

$F_{9,178}$=5.05; p<0.001; Std. Err=0.3213

R^2 = 0.20; Adj. R^2=0.16

Sample sizes are SYL (39), ADU (46), CHI (39), 2ndGEN (29), WHI (45).

Table 22. Multiple linear regression matrix showing determinants of total oestradiol index

N	193	193	191	188	192	189	184
Adj. R2	0,01	0,00	0,01	0,01	0,02	0,01	0,01
				Std. Coef. (beta)			
Age	..	-0.04 ns	..	..	..	..	-0.08 ns
BMI	..	..	0.09 ns	..	..	..	0.15 ns
Triceps	..	..	..	0.01 ns	..	..	-0.09 ns
Height	..	..	..	..	-0.15 ns	..	-0.13 ns
Menarche	..	..	..	..	..	0.00 ns	0.04 ns
Group (SYL as reference)							
ADU	0.09 ns	0.11 ns	0.07 ns	0.11 ns	0.09 ns	0.09 ns	0.11 ns
CHI	-0.04 ns	-0.03 ns	-0.06 ns	-0.04 ns	-0.03 ns	-0.04 ns	-0.04 ns
2ndGEN	-0.12 ns	-0.12 ns	-0.14 ns	-0.12 ns	-0.11 ns	-0.13 ns	-0.14 ns
WHI	0.01 ns	0.01 ns	-0.02 ns	-0.00 ns	0.09 ns	-0.02 ns	0.09 ns

Note: None of the models is significant.

Table 23. Linear regression model for mean total oestradiol index

Characteristic	Unstardised coefficient (B)	SE of B	Standardised coeficient (beta)	t value	p
Constant	25.40	14.43	..	1.76	0.08
Age	-0.09	0.11	-0.08	-0.84	0.40
BMI (kg/m^2)	0.20	0.15	0.15	1.28	0.20
Triceps (mm)	-0.09	0.11	-0.09	-0.77	0.44
Height (cm)	-0.11	0.09	-0.13	-1.32	0.19
Age at menarche (yrs)	0.18	0.35	0.04	0.50	0.62
Groups					
ADU	1.77	1.63	0.11	1.09	0.28
CHI	-0.61	1.57	-0.04	-0.39	0.70
2ndGEN	-2.31	1.61	-0.14	-1.44	0.15
WHI	1.36	1.81	0.09	0.75	0.45

Notes: dummy SYL as reference group

$F_{9,175}$=1.20; p>0.05; Std. Err=6.3576
R^2= 0.058; Adj. R^2=0.010

Sample sizes are SYL (41), ADU (42), CHI (35), 2ndGEN (31), WHI (45).

Figure 9. Age at menarche vs age at migration (First generation groups categorised according to age on arrival irrespective of menarcheal status <= 16 / 17+ years criteria).

Hypotheses testing

HYPOTHESIS A: Poor conditions experienced during infancy and childhood will result in adult women having lower average baseline levels of ovarian steroid hormones (progesterone and oestradiol) than those living in more affluent conditions.

Prediction A: Sylheti women and adult migrants will have lower ovarian steroids than child migrants, second-generation women and white women.

Multiple linear regression models show significant differences in progesterone levels between groups (R^2 = 0.21; p<0.01; Adj. R^2 = 0.16). Average luteal progesterone values are significantly higher in the child migrant, second generation and white groups (75, 81 and 103%, respectively) compared to those in the Sylheti and adult migrant groups irrespective of anthropometric and reproductive variables controlled for in the model (Table 21). Similar results are obtained for average peak luteal progesterone values (R^2 = 0.22; p<0.001; Adj. R^2 = 0.18). Second generation and white women have significantly higher values for this index (49% and 72%, respectively) compared to women in the Sylheti group. First generation women do not differ significantly from Sylhetis in this respect. Moreover, age at menarche contributes significantly to variation in this progesterone index; representing a 9.1 increase in pg/ml for every year menarcheal age is shortened (Tables 24 & 25; Figure 10). Figure 11 and 12 show average group progesterone profiles and progesterone indices, respectively.

Multiple linear regression models show no significant differences in total (R^2 = 0.06; p>0.05; Adj. R^2 = 0.01), follicular (R^2 = 0.06; p>0.05; Adj. R^2 = 0.01), luteal (R^2 = 0.05; p>0.05; Adj. R^2 = 0.003) or mid-cycle oestradiol (R^2 = 0.04; p>0.05; Adj. R^2 = 0.005) levels between groups (Tables 23, 26, 27 & 28). Figures 13 and 14 show average group oestradiol profiles and oestradiol indices, respectively.

Table 24. Multiple linear regression showing determinants for highest luteal progesterone value index

N	196	196	194	190	194	190	186
Adj. R2	0,09	0,10	0,13	0,14	0,08	0,12	0,18

			Std. Coef. (beta)				
Age	..	-0.15 ns	..	..	..	..	-0.01 ns
BMI	..	..	-0.24 **	..	..	..	-0.07 ns
Triceps	..	..	..	-0.25 **	..	..	-0.16 ns
Height	..	..	..	..	0.06 ns	..	0.12 ns
Age at menarche	..	..	..	..	..	-0.22 **	-0.23 **

Group (SYL as reference)

ADU	0.09 ns	0.16 ns	0.18 ns	0.17 ns	0.09 ns	0.02 ns	0.13 ns
CHI	0.18 *	0.20 *	0.24 **	0.24 **	0.18 *	0.09 ns	0.15 ns
2ndGEN	0.25 **	0.23 **	0.30 **	0.30 **	0.24 **	0.16 **	0.21 **
WHI	0.37 **	0.43 **	0.39 **	0.39 **	0.33 **	0.35 **	0.29 **

*p<0.05; **p<0.01

Table 25. Linear regression model for highest luteal progesterone value index

	Unstardised coefficient (B)	SE of B	Standardised coeficient (beta)	t value	p
Constant	1.97	0.57	..	3.45	0.00
Age	-0.00	0.01	-0.01	-0.12	0.90
BMI (kg/m²)	-0.00	0.01	-0.07	-0.69	0.49
Triceps (mm)	-0.00	0.01	-0.16	-1.10	0.19
Height (cm)	0.00	0.00	0.12	1.37	0.17
Age at menarche (yrs)	-0.04	0.01	-0.24	-3.27	**0.00**
Groups					
ADU	0.08	0.06	0.13	1.34	0.18
CHI	0.10	0.06	0.15	1.67	0.10
2ndGEN	0.16	0.07	0.21	2.47	**0.01**
WHI	0.19	0.07	0.29	2.67	**0.00**

Notes: dummy SYL as reference group

$F_{9,177}$=5.40; p<0.001; Std. Err=0.2473

R^2 = 0.22; Adj. R^2=0.18

Sample sizes are SYL (39), ADU (46), CHI (39), 2ndGEN (29), WHI (45).

Figure 10. Highest luteal progesterone value vs. Age at menarche (all groups)
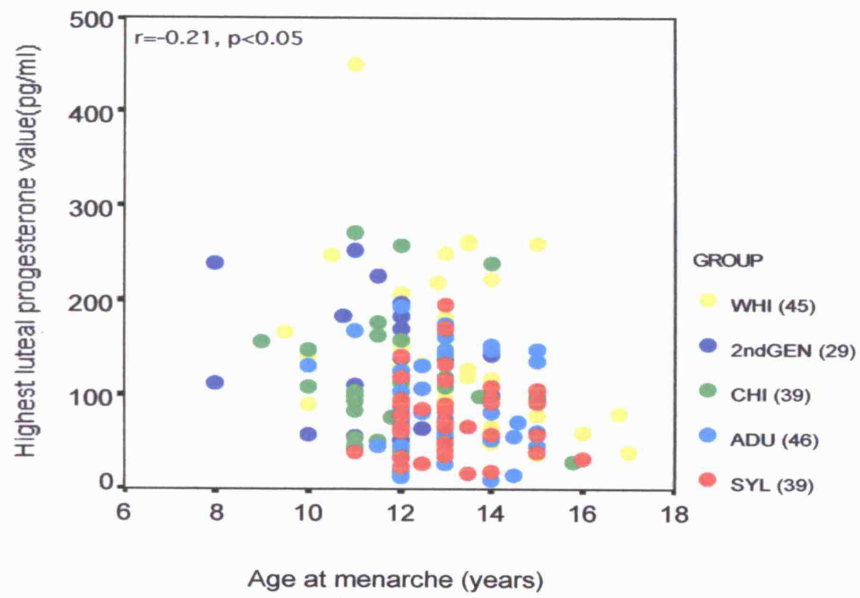
Figure 11. Average luteal progesterone profiles by group

Note: Confidence intervals are omitted for clarity

Legend: SYL (39), ADU (46), CHI (39), 2ndGEN (29), WHI (45)

X-axis: Cycle day relative to estimated day of ovulation (0)

Y-axis: Salivary progesterone (pg/ml)

143
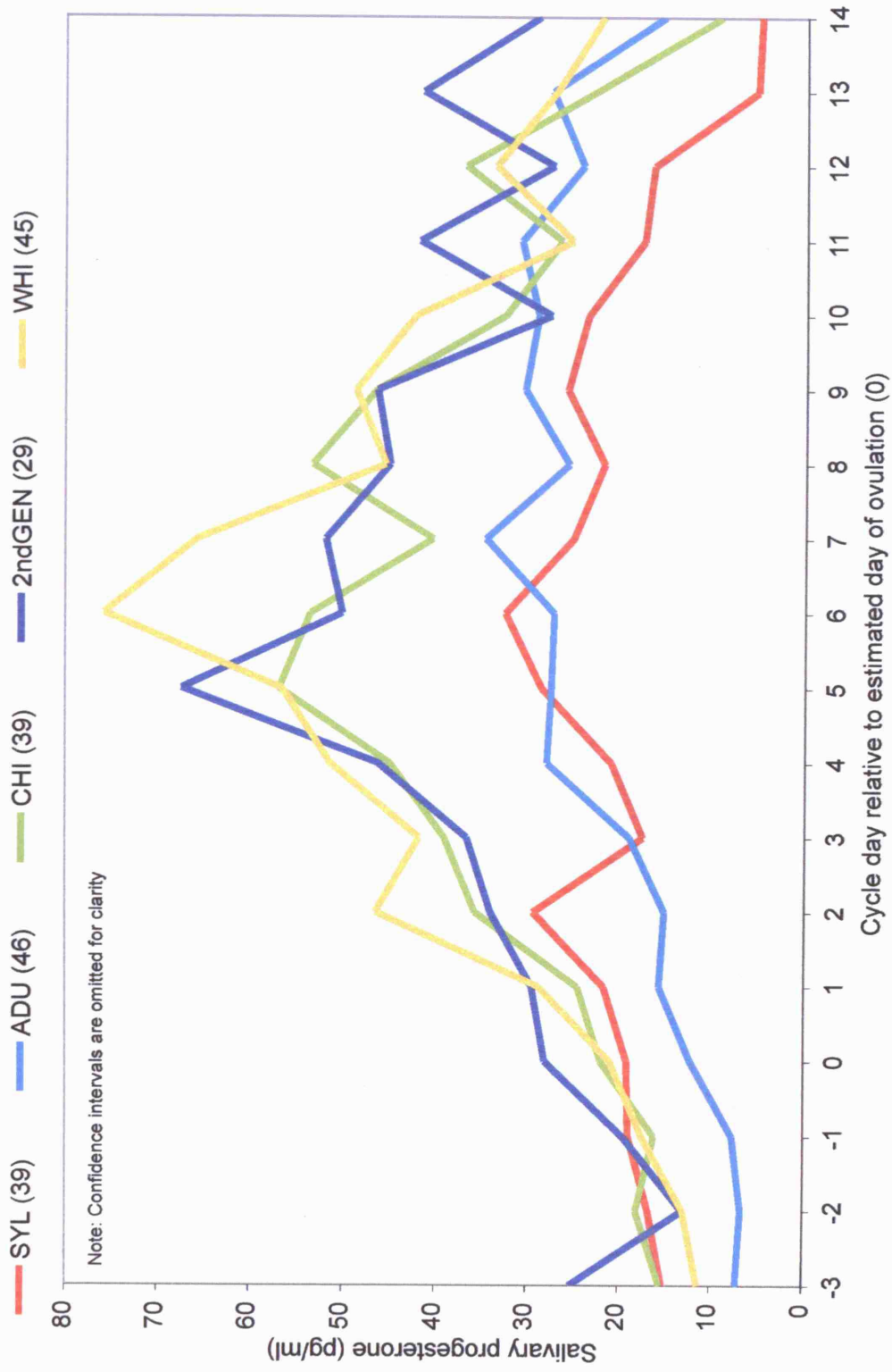
Figure 12. Average progesterone indices by group

144
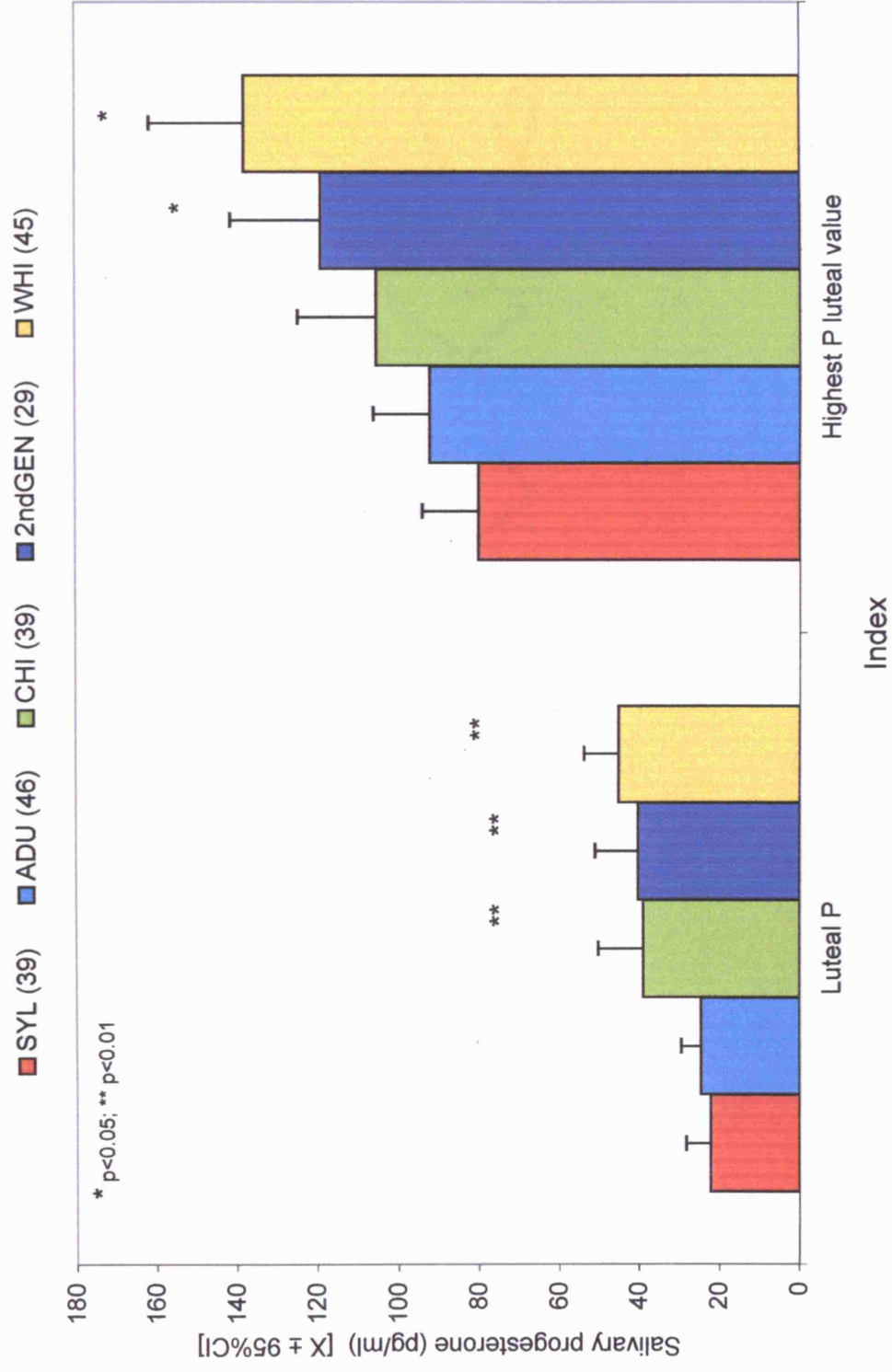
Figure 13. Average oestradiol profiles by group

Note: Confidence intervals are omitted for clarity

SYL (41)   ADU (42)   CHI (35)   2ndGEN (31)   WHI (45)

Salivary oestradiol (pg/ml)

Cycle day relative to estimated day of ovulation (0)

145
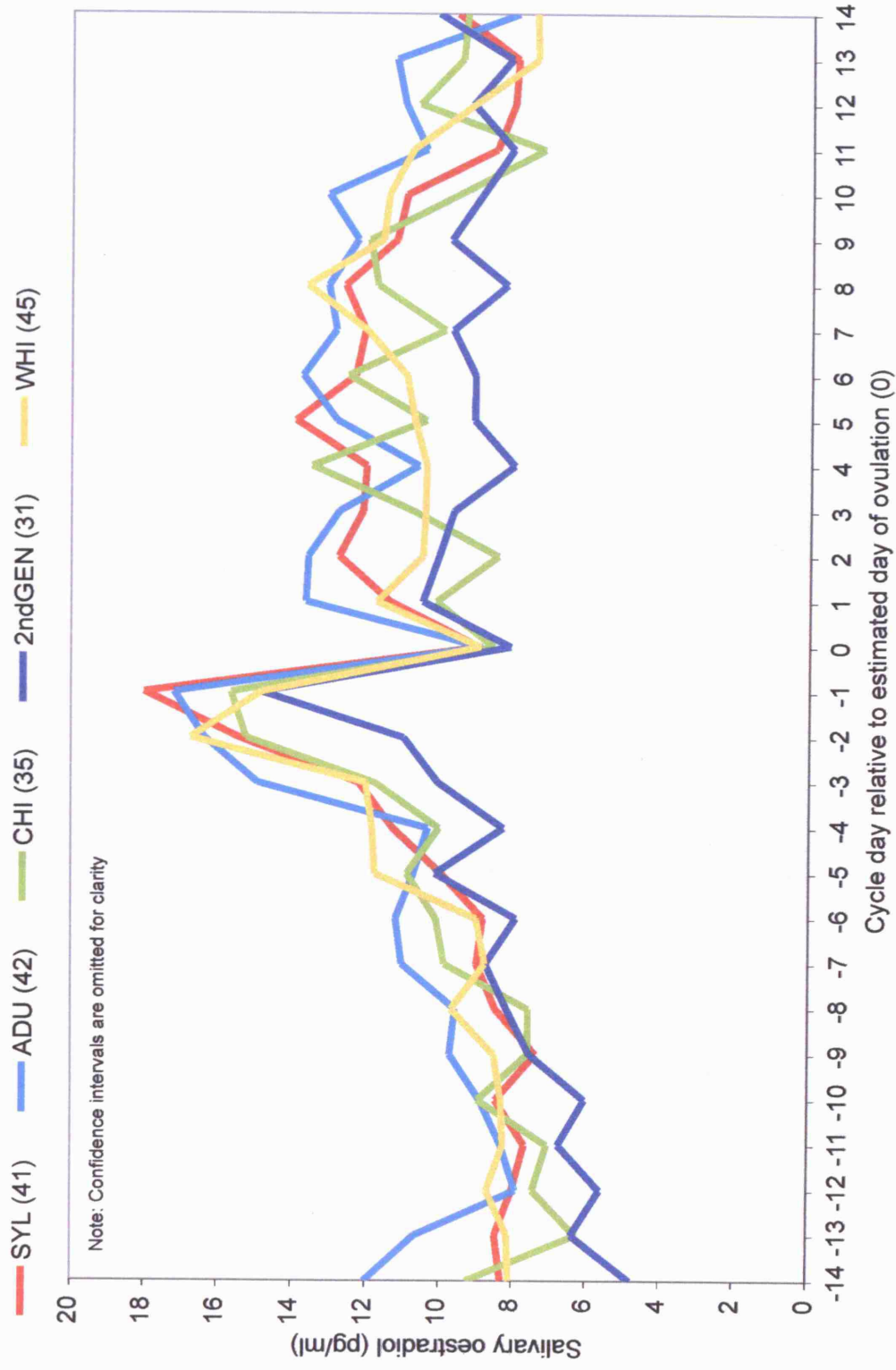
Figure 14. Average oestradiol indices by group
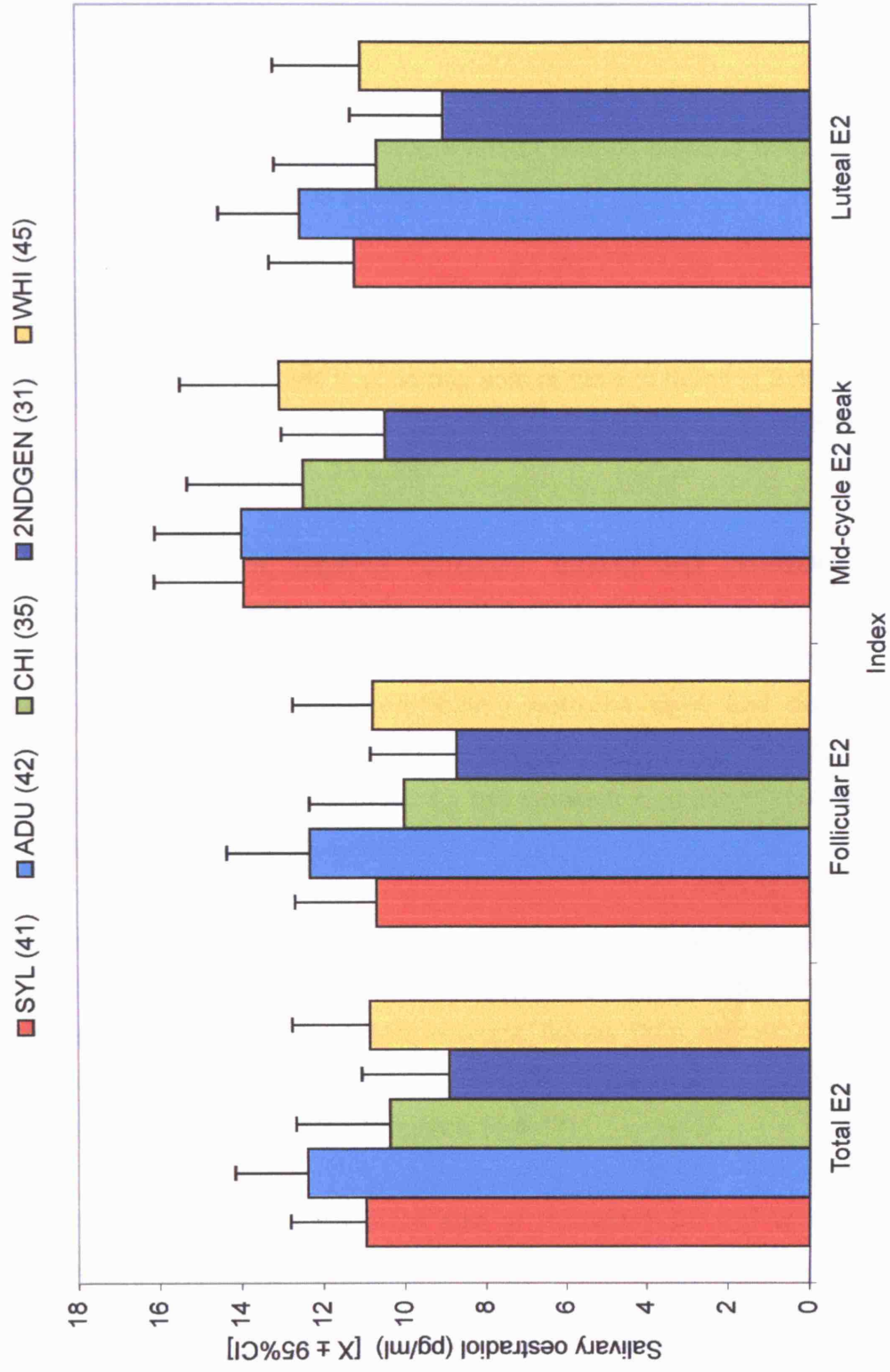
HYPOTHESIS B: A positive change in environmental conditions that impacts developmental tempo will be reflected in enhanced reproductive hormonal function; migrants who move to an affluent environment while growth and development is ongoing, will have higher ovarian steroid levels than sedentees.

Prediction B: Child migrants will have levels of ovarian steroids that are negatively correlated with age at migration.

Multiple linear regression models show that average luteal progesterone levels are significantly higher in child migrants relative to those in Sylheti women. However, the same is not true for average peak luteal progesterone values (Tables 21 & 25).

There is a significant negative correlation among first generation migrants between average luteal progesterone values and age at migration ($r = -0.24$, $p = 0.03$) with higher values among younger arrivals (Figure 15). When discriminating between child and adult migrant groups (defined according to age at entry into UK $\leq 16/17+$ years criteria), the correlation is significant for the former ($r = -0.28$, $p = 0.04$) but not for the later ($r = 0.16$, $p=0.33$).

A one-way ANOVA indicates that first generation women who migrated in infancy (aged 0-2) have significantly higher average luteal progesterone and peak luteal progesterone values than women who migrated at a later stage ($F_{3,81} = 3.30$, $p = 0.02$ for luteal P; $F_{3,80} = 2.90$, $p = 0.04$ for peak luteal P index) (Figures 16 & 17).

There was no significant effect of age at migration on any of the oestradiol indices among first-generation women (total $r = 0.15$, $p = 0.18$; follicular $r = 0.16$, $p = 0.14$; luteal $r = 0.13$, $p = 0.27$; mid-cycle peak $r = 0.09$, $p = 0.43$) (Figure 18).

Figure 15. Luteal progesterone index (pg/ml) vs age at migration (1st generation groups categorised according to age on arrival irrespective of menarcheal status (<= 16 yrs /17+ years criteria).
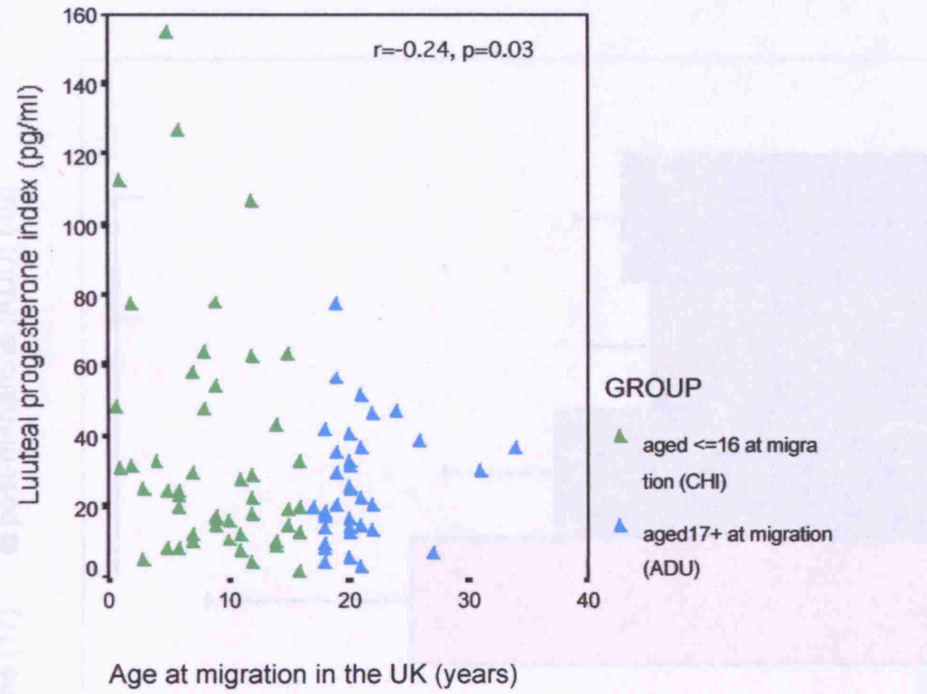
C

Figure 16. Average progesterone indices by categories of age at migration to the UK (1st generation groups)

0-2 y (5)   3-8 y (17)   >9 y < menarche (17)   post-menarche (ADU) (46)

* p<0.05

Salivary progesterone (pg/ml) [X ± 95%CI]

Luteal P   Progesterone Index   Highest luteal P value

149
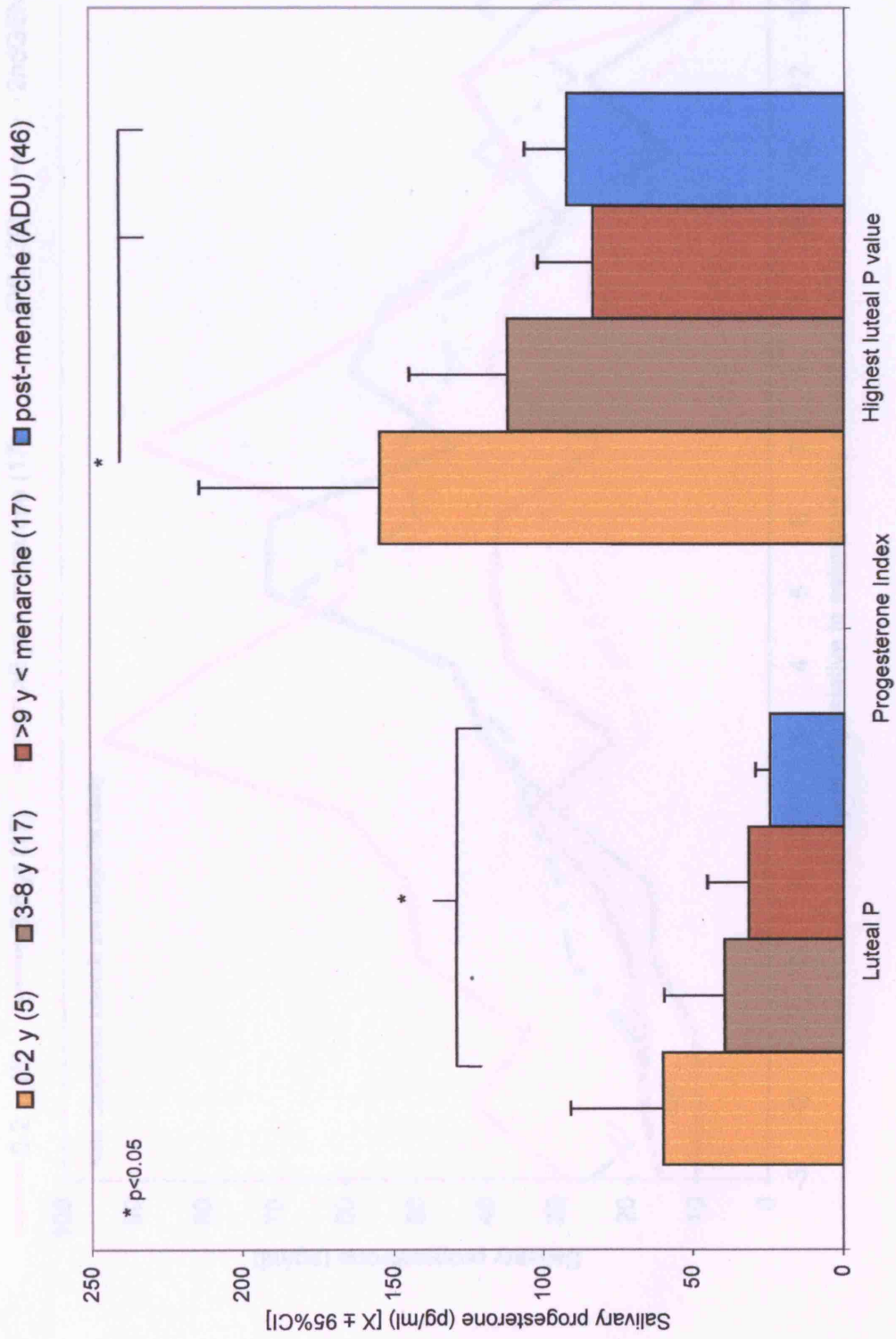
C

Figure 17. Average luteal progesterone profiles by categories of age at migration in the UK (Child migrants only)

Note: Confidence intervals are omitted for clarity

Legend:
- 0-2 yr (5)
- 3-8 yr (17)
- >9 yr < menarche (17)
- SYL (39)
- 2ndGEN (29)

Y-axis: Salivary progesterone (pg/ml)
X-axis: Cycle day relative to estimated day of ovulation (0)
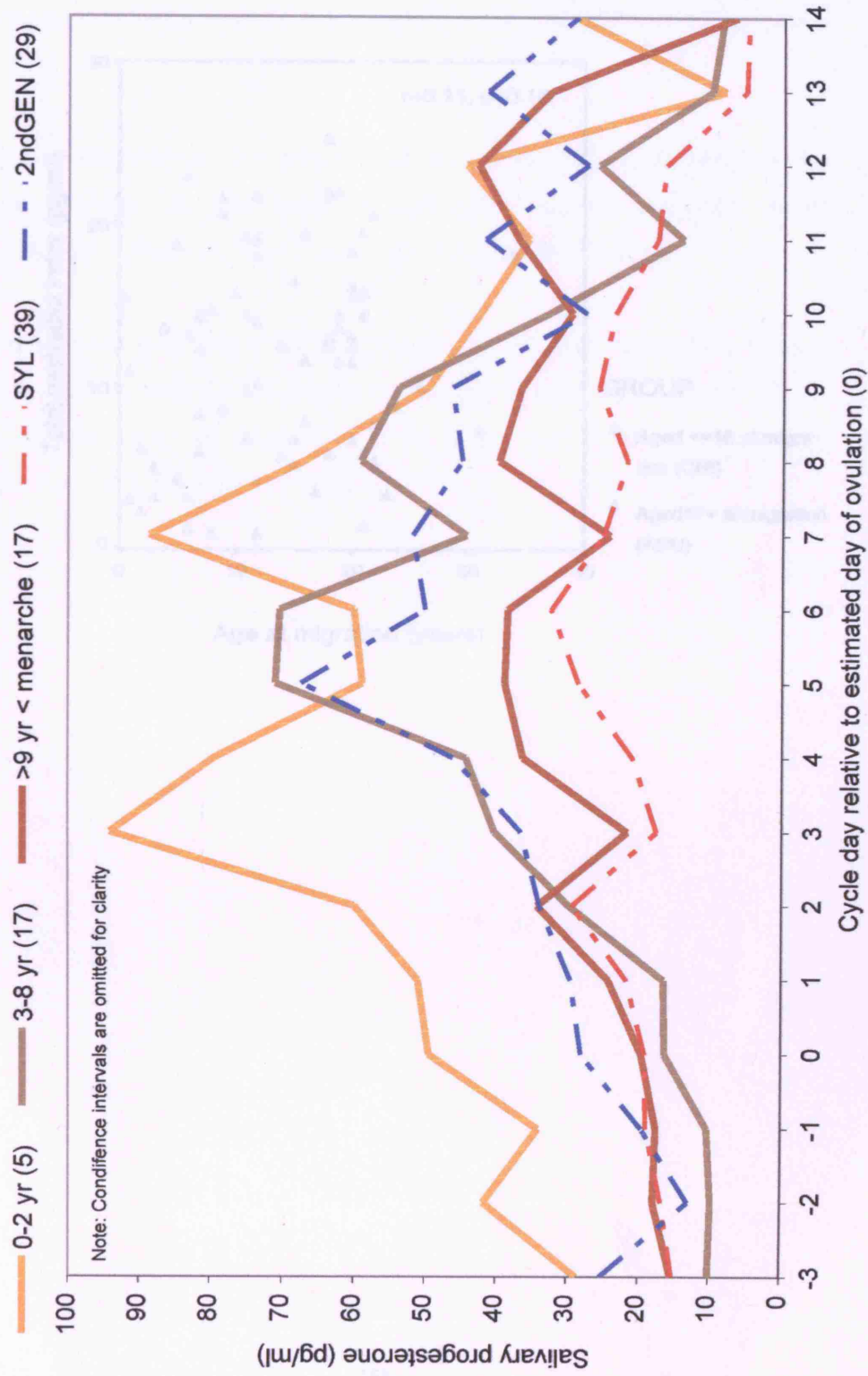
Figure 18. Total oestradiol index (pg/ml) vs age at migration (First generation groups categorised according to age on arrival irrespective of menarcheal status (<= 16 yrs /17+ years criteria).
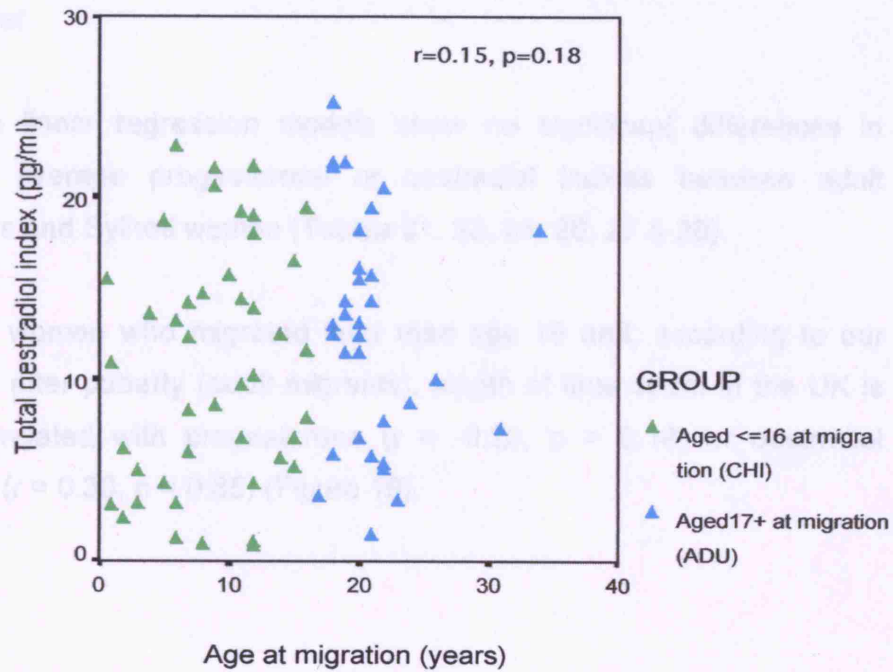
HYPOTHESIS C: Alterations in conditions after maturation will not modify the *baseline* set points established during early life.

Prediction C: Adult migrants will have steroid levels that are comparable to Sylheti sedentees even if their current adult energetic conditions are dissimilar.

Multiple linear regression models show no significant differences in neither average progesterone or oestradiol indices between adult migrants and Sylheti women (Tables 21, 23, 25, 26, 27 & 28).

Among women who migrated later than age 16 and, according to our criteria, after puberty (adult migrants), length of time spent in the UK is not correlated with progesterone (r = -0.20, p = 0.18) or oestradiol indices (r = 0.30, p = 0.85) (Figure 19).

Figure 19. Luteal progesterone and total oestradiol indices vs. time spent in the UK (adult migrants only, defined as entering the UK older than 17 yrs).

Table 26. Linear regression model for follicular oestradiol index

Characteristic	Unstandised coefficient (B)	SE of B	Standardised coeficient (beta)	t value	p
Constant	23.79	14.97	..	1.59	0.11
Age	-0.01	0.11	-0.01	-0.13	0.90
BMI (kg/m^2)	0.19	0.16	0.14	1.18	0.24
Triceps (mm)	-0.11	0.12	-0.11	-0.97	0.33
Height (cm)	-0.12	0.09	-0.13	-1.32	0.19
Age at menarche (yrs)	0.21	0.36	0.04	0.58	0.56
Groups					
ADU	1.71	1.69	0.10	1.02	0.31
CHI	-0.61	1.63	-0.04	-0.37	0.71
2ndGEN	-1.88	1.67	-0.10	-1.13	0.26
WHI	1.38	1.88	0.09	0.74	0.46

Notes: dummy SYL as reference group

$F_{9,175}=1.16$; p>0.05; Std. Err=6.599
R^2 = 0.056; Adj. R^2=0.008

Sample sizes are SYL (41), ADU (42), CHI (35), 2ndGEN (31), WHI (45).

Table 27. Linear regression model for mid-cycle oestradiol peak index

Characteristic	SE of B	Standardised coeficient (beta)	t value	p
Constant	17.39	..	1.86	0.06
Age	0.13	-0.01	-0.11	0.92
BMI (kg/m^2)	0.19	0.03	0.24	0.81
Triceps (mm)	0.14	-0.00	-0.03	0.98
Height (cm)	0.10	-0.15	-1.50	0.14
Age at menarche (yrs)	0.42	0.07	0.86	0.39
Groups				
ADU	1.96	-0.01	-0.09	0.93
CHI	1.89	-0.06	-0.64	0.52
2ndGEN	1.94	-0.15	-1.63	0.10
WHI	2.18	0.03	0.24	0.81

Notes: dummy SYL as reference group

$F_{9,175}$=0.89; p>0.05; Std. Err=7.664
R^2 = 0.044; Adj. R^2=-0.005

Sample sizes are SYL (41), ADU (42), CHI (35), 2ndGEN (31), WHI (45).

Table 28. Linear regression model for luteal oestradiol index

Characteristic	Unstandised coefficient (B)	SE of B	Standardised coeficient (beta)	t value	p
Constant	26,41	15,69	..	1,68	0,09
Age	-0,16	0,12	-0.12	-1,34	0,18
BMI (kg/m^2)	0,19	0,17	0,13	1,13	0,26
Triceps (mm)	-0,05	0,12	-0.00	-0,43	0,67
Height (cm)	-0,10	0,09	-0.11	-1,12	0,26
Age at menarche (yrs)	0,13	0,38	0,03	0,35	0,73
Groups					
ADU	1,89	1,77	0,11	1,07	0,29
CHI	-0,65	1,71	-0.04	-0,38	0,71
2ndGEN	-2,73	1,75	-0.15	-1,56	0,12
WHI	1,25	1,97	0,07	0,63	0,53

Notes: dummy SYL as reference group

$F_{9,175} = 1.07$; $p > 0.05$; Std. Err=6.91
$R^2 = 0.052$; Adj. $R^2 = 0.003$

Sample sizes are SYL (41), ADU (42), CHI (35), 2ndGEN (31), WHI (45).

Discussion

Relationship between anthropometric, reproductive and endocrine variables.

The negative association between luteal progesterone and BMI and triceps skinfolds is rather puzzling. Previous reports on the association of body composition measurements and steroid levels have so far been in the context of *change* in energy balance (gain or weight loss due to ecological or self-imposed factors), which by definition implies relative comparisons between at least two points in time. In such studies, women show significantly lower steroid levels after a period of weight loss or compared to women who did not lose weight (see table 12). Never has the direct association between reproductive steroid levels and a single measurement of an individual's BMI or skinfolds at any point in time been reported before, rendering it impossible to make comparisons with the results found here. Since most previous work has linked low steroid levels to measurements indicative of detrimental conditions, it appears counterintuitive that low BMI is associated with high luteal progesterone levels. However, it can be argued that this correlation as it stands is of no biological relevance, for a sole measurement of an individual's BMI or skinfold serves no function in describing her energetic history, unless it is judged against a reference, be it an intra- or an inter- individual one. It still remains somewhat intriguing and it would be interesting to check in future (and past) studies if the correlation holds in other datasets.

The finding that age at menarche is significantly correlated with mean luteal progesterone confirms previous observations that women who mature earlier exhibit higher reproductive levels as adults (Vihko & Apter, 1984; Apter & Vikho, 1985; Apter, 1996).

The positive association between final height and age at menarche has been observed elsewhere (Proos *et al.*, 1991b, a; Proos, 1993; Cole, 2000; Adair, 2001) and is partly explained, as the result of increased steroid levels during puberty that promote epiphyseal fusion of the long

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bones and the consequent halting of linear growth (Porcu et al., 1994; Cutler, 1997; Juul, 2001; Frank, 2003). Because of this pattern of skeletal development, late maturers grow for relatively longer and are likely to reach higher final statures than women who attain menarche at younger age and stop growing earlier (Okasha et al., 2001).

Timing of sample collection and ultradian/circadian variance

Ultradian and circadian patterns are among the numerous recognised sources of inter- and intra individual variation in salivary steroid levels. (Ellison, 1988). Steroids are released by the gonads and adrenals in a periodic (circadian and ultradian) fashion as well as in discrete (episodic or pulsatile) mode; plasma measurements in the laboratory have shown secretion peaks as frequent as every two hours (Kottler et al., 1989). However, the frequency, timing and amplitude of these pulses vary dramatically both between and within individuals, with patterns of variation that may be related to physiological and emotional factors (Ellison, 1988; Veldhuis et al., 1988; Kottler et al., 1989); some individuals even failing to show detectable circadian patterns at all (Aedo et al., 1981). In conjunction with a late luteal ultradian pattern (changes in the frequency and amplitude of secretion pulses) (O'Rourke, 1990), reproductive steroids exhibit a circadian pattern, with a tendency to higher morning than evening levels throughout the menstrual cycle (Ellison, 1988; Kottler et al., 1989).

These sources of variation can introduce a significant probability of error in any attempt to characterise ovarian hormonal function from only a few samples. However, it is well documented that since synchronising sampling collection to individual pulsatile patterns of steroid secretion - especially under field conditions- is unfeasible, the collection of multiple serial samples across the menstrual cycle in order to characterise individual hormonal profiles contributes to diminish the impact of circadian and ultradian variation, as well as other "random" intra-individual variation (Ellison, 1988). In fact, it has been shown that the

steady rise in plasma progesterone levels observed during the luteal phase can completely mask the circadian rhythm during such phase (Aedo *et al.*, 1981).

In the present study, hormonal profiles and indices were derived from daily samples over an entire menstrual cycle. Moreover, although women are likely to have differed with regard to the time of the day when they collected their samples, either from one day to the next, or from individual to individual, it can be expected that this would have been the case in all five study groups and therefore the variation due to circadian and ultradian patterns is likely to have been randomly distributed among groups.

Progesterone levels

The developmental hypothesis outlined by Ellison (1996) and discussed in the introduction predicts that populations subject to adverse energetic conditions (due to nutrition, physical activity or epidemiological factors) will have a slower maturation rate and lower levels of ovarian function during adulthood than populations that enjoy energetic abundance. The study presented here provides the first available data for chronic variation in ovarian function in a population that is not living under extreme ecological conditions (i.e. under no obvious nutritional and/or physical energetic stress), but living under moderate immunological stress, and the first to support empirically the predictions derived from the developmental hypothesis. Bangladeshi immigrants who grew up in the UK under more affluent conditions have higher levels of progesterone and enhanced growth trajectories with earlier maturation compared to women still living in Bangladesh, where poorer environmental conditions are reflected in low progesterone levels and delayed maturity.

The negative correlation between age at menarche and both progesterone indices (luteal P and highest luteal P value) suggests that

women with fast maturation trajectories not only have higher overall hormone levels but also a higher capacity for progesterone secretion. These differences in secretion could be related to variation in ultradian patterns of progesterone release and ultimately be evidence of variation in hypothalamic-pituitary-ovary (HPO) axis settings (Lipson & Ellison, 1992). These findings complement the studies by Apter and Vikho (1985) showing that earlier maturation leads to enhanced adult steroid levels. This is also the first ecological study of ovarian function where an association between menarcheal age and progesterone levels is shown within the same population rather than from a correlation extracted from independent data sources (Ellison, 1996; Jasienska & Thune, 2001).

Despite the small sample sizes in each of the three age-categories of child migrants (infancy, childhood and peri-menarche), comparisons of progesterone indices between these groups point to the period of infancy as a sensitive stage during which the effects of an improved environment have the strongest impact on adult outcomes of reproductive steroid function. Elevations in progesterone levels are less apparent when a change in environmental conditions is experienced during childhood until around the time of adrenarche, and are almost non-existent in the later peri-menarcheal period. Although the precise role of adrenal steroids in reproductive and physical maturation is not fully understood, it is known that adrenal steroids exhibit a developmental profile with distinctive shifts in circulating levels from mid-childhood through early adulthood. There is also evidence that variation in these hormones due to environmental quality corresponds to differences in adult reproductive function as measured by levels of gonadal steroids, and that this association may be mediated through variation in regulatory set-points at the hypothalamic level (Worthman, 1999). The magnitude of the effect of age of exposure to improved conditions can be gauged by the following comparisons: progesterone indices of women who migrated to the UK as infants are similar to those of UK-born women, whereas levels of those arriving

close to adolescence are indistinguishable from those who migrated as adults and those of Sylhet sedentees (Figure 16).

That adult migrants and Sylhet sedentees did not differ in baseline progesterone levels despite their contrasting current environments, physical activity patterns and body composition measures, may be taken as evidence of the "robustness" of those physiological adaptations established during early life that determine set points for ovarian function. This finding is in agreement with the predictions of life history theory that formative conditions determine the level of reproductive function that favours the most profitable strategy under certain set of energetic conditions.

The fact that height and menarcheal age as proxies for tempos of growth and maturation, in addition to ovarian hormones, appear affected by conditions at similar stages of development is compelling evidence in favour of the hypothesis that reproductive function is linked to developmental tempo. In particular, the results here suggest that the period of infancy is a highly sensitive one in gauging environmental quality.

Several other studies have also identified the period of early post-natal life as critical for the establishment of growth and maturation trajectories. (Cooper *et al.*, 1996; Coe & Shirtcliff, 2004). For example, fast growth trajectories initiated at birth and evident before two years of age are associated with an early menarche (Adair, 2001). Similarly, secular increases in height already achieved by age two are carried through to adulthood, and are thought to be the result of the interaction of pre-natal factors and the quality of the diet and exposure to infection in the early post-natal period (Cole, 2000). Growth at this stage is driven by growth hormone (GH) for which receptors on the growth plates of the long bones are regulated directly by nutrition (Karlerberg *et al.*, 1994). Retrospective studies have also indicated that a high-energy diet during

infancy is associated with a faster tempo of growth and maturation (Berkey *et al.*, 2000; Koo *et al.*, 2002). Additionally, there is evidence for a shift in regulatory and secretion patterns in various metabolic and endocrine axes during infancy, possibly in conjunction with brain development (Worthman, 1999).

Although infancy appears to be an essential period for monitoring environmental conditions and determining later trajectories, there is evidence that maturation and growth continue to be plastic in later childhood. For example, numerous migrant and refugee studies show that − improvements in adverse childhood conditions that were the cause of growth faltering (such as poor nutrition, chronic infection and psychosocial stress) lead to catch-up growth and growth outcomes that are equivalent to those of the native, more affluent population (Goel *et al.*, 1981; Mjones, 1987; Schumacher *et al.*, 1987; Proos *et al.*, 1991a; Yip *et al.*, 1992; Yip *et al.*, 1993). Nutritional intervention and prospective and retrospective studies give further examples of how the tempo of growth and maturation can be affected by conditions during childhood. For example, a high animal protein intake during childhood is associated with an earlier peak growth during adolescence, while a higher consumption of calories and animal protein (controlled for body size) two years before peak growth results in a higher peak growth velocity (Berkey *et al.*, 2000).

The importance of the timing of changes in the quality of the environment and its impact on developmental trajectories is illustrated in a longitudinal study of adopted Indian girls in Sweden. In that study, the age at which girls arrived in Sweden determined their subsequent patterns of growth and maturation. Girls adopted close to adolescence showed accelerated growth, hastened maturation, and consequently, smaller than expected final stature compared to girls adopted in early childhood who showed equally early maturation but taller statures. In both cases, adopted girls showed much younger menarcheal ages than

their Swedish peers (2-3 years) (Proos *et al.*, 1991b, 1992). These findings suggest that growth and maturation tempos are not necessarily equally or simultaneously affected by changes in conditions, but rather that there are specific critical periods for each of them. Unfortunately, the present study lacks the longitudinal data to analyse which components of the growth and maturation trajectories (e.g. height velocity, age at peak velocity, onset of puberty, etc.) were modified among Bangladeshi women after migration to the UK, and of the role of age at migration on such changes.

It remains unclear how growth and maturation rates (and by implication ovarian function) are related, established and modified in terms of susceptible periods and underlying mechanisms. However, it is evident from the coordination of the final phases of physical growth with reproductive maturation that both processes interact. Ellison (1981) has suggested that this interaction has a critical adaptive value in ensuring that pelvic skeletal maturation is appropriately timed to ensure a safe delivery following a potential early conception (Ellison, 1981c, 1982).

Proposed mechanisms for the developmental effect on ovarian function

The metabolic axis as an integrator of both the acute and chronic energetic cues from the environment and as coordinator of the allocation of the available energy into growth, maintenance and reproduction processes is a likely candidate through which developmental trajectories may be established and/or modified. In principle, the quality of the environment during the formative years in terms of infection, physical activity and nutrition, could determine the basic parameters of a metabolic blueprint that would govern the trajectory of development. This would influence the tempo of maturation and consequently, baseline levels of ovarian adult function.

There is considerable evidence to show that the metabolic hormones particularly insulin, insulin-like growth factors (IGFs) and leptin are indeed implicated in determining the timing of the onset of pubertal development, the tempo of the adolescent growth spurt, and the concurrent increase in adrenal steroid levels (Hindmarsh et al., 1988; Smith et al., 1989; Apter, 1997; Chehab et al., 1997; Wilson, 1998; Foster & Nagatani, 1999; Ong et al., 1999). For example, plasma insulin levels, IGF-I and leptin are known to rise significantly just before puberty (Hiney et al., 1991; Suter et al., 2000). Similarly, apart from the indirect impact of the metabolic hormones on reproductive function through their association with maturation tempo, the metabolic hormones are also implicated in the regulation of adult ovarian function directly via their actions on the HPO axis (Poretsky et al., 1999). Insulin and IGF enhance the steroid production by granulosa and theca cells in the ovary, stimulate oocyte maturation and follicular growth, and also stimulate GnRH secretion in the hypothalamus (Poretsky et al., 1985; Samoto et al., 1993; McGee et al., 1996; Willis et al., 1996; Karlsson et al., 1997; Duleba et al., 1998; Poretsky et al., 1999).

In the context of this study, it is predicted that women who developed in Bangladesh would have a slower development trajectory as a consequence of a metabolic blueprint adjusted to parameters of poor conditions compared to the blueprint of energy affluence among women in the UK. Unfortunately there are no data on population differences in metabolic hormones to support this hypothesis. However, the increased susceptibility to Type II diabetes among Bangladeshi immigrants in the UK may be an indicator of a metabolic blueprint set at low energy parameters that, in conditions of affluence, has turned maladaptive (Mather & Keen, 1985; McKeigue et al., 1988, 1991; McKeigue, 1996; Erens et al., 2001; Holt, 2004).

Since regulation of the metabolic axis may vary through the lifespan (Holt, 2002), and the effects of metabolic hormones on the reproductive

system seem more pronounced at certain stages of development than others (e.g., the pre-adolescent period) (Hindmarsh et al., 1988; Hiney et al., 1991; Apter, 1997; Suter et al., 2000), the timing of changes in energetic conditions would determine, in part, their effects on maturation rates and by implication on ovarian function. Presumably, the closer to the end of the growth and maturation processes the changes occur, the less likely it is that developmental patterns and set points for ovarian function can be significantly modified by the metabolic axis. The differences in progesterone levels, growth and maturational ages found in the present study among the women who migrated to the UK at different stages of development, and the seemingly decreased responsiveness to changes in the environment with age are consistent with these predictions.

In conclusion, it is proposed that energy availability during the formative years can influence the tempo of maturation via the metabolic hormones, and, consequently, levels of adult ovarian function. Following from this, chronic energetic conditions would establish a basic pattern of energy allocation to reproductive function, around which adjustments to short-term fluctuations in energy availability can be made. The final outcome of such fine-tuned regulation would be to increase or decrease the probability of pregnancy according to the prevailing conditions in order to optimise reproductive effort and ultimately increase fitness (Ellison, 1996; Lipson, 2001).

Oestradiol levels

Inter-population differences

The lack of differences in oestradiol levels between women in Bangladesh and women in the UK (as measured by total, follicular, mid-cycle peak and luteal indices), is in contrast with previous findings of lower salivary oestradiol levels in energetically stressed populations

compared to those in Western affluent conditions. For instance, Lese women of the Ituri Forest, Democratic Republic of the Congo (DRC) (Bentley *et al.*, 1988), rural Aymara women in Bolivia (Bentley *et al.*, 2000; Horton, 2003) and Tamang women in Nepal (Panter-Brick *et al.*, 1996) have been found to have considerably lower salivary oestradiol levels than middle-class white women living in urban affluent environments in the USA and the UK.

It could be argued that the hormonal discrepancies between the groups cited above and the Bangladeshis arise from the more energetically stressful lifestyles of the former populations. The Lese, for example, are subsistence horticulturalists characterised by a very high energy expenditure and seasonal fluctuations in dietary intake and hence energy balance (Bentley *et al.*, 1988; Bailey *et al.*, 1992). This group is continuously exposed to infectious and parasitic agents in their environment (Dietz *et al.*, 1989), have high rates of sexually-transmitted diseases (Bailey & Aunger, 1995) and no access to sanitary facilities or health services. They, therefore, represent the extreme of the ecological continuum. The Aymara women live at altitudes of around 4000m and depend on seasonal agriculture for most of their subsistence. They suffer from poverty, poor nutritional intake and also lack access to electricity, clean water, proper sanitation and health care. The fact that their steroid levels compare to those of poor populations living at lower altitude makes it unlikely that hypoxia is the sole cause of their suppressed hormone levels (Vitzthum *et al.*, 1994). The Tamang women are also a subsistence agro-pastoralist group living in very basic conditions at 1900m in the foothills of the Himalayas who show very high levels of physical activity and experience marked seasonal variation in workloads (Panter-Brick *et al.*, 1993). In contrast, compared to these populations, Sylheti women are relatively better off. As has been discussed previously (see Chapter 2), participants in the present study belong to the middle-class in Bangladesh and, although their living standards contrast with those in the UK, they by no means suffer food

insecurity or significant seasonal variation in dietary intake. Most Sylheti women have a sedentary lifestyle with low energy expenditure and are not engaged in heavy physical activities relating to their subsistence. Thus the only common denominator between this group, the Lese, the Tamang and the Aymara would be the limited access to, and quality of, sanitary and health services, but even then Sylhetis are affected to a much lesser degree than the other two populations. The significantly lower chronic oestradiol levels compared to Western women observed in the Lese, the Aymara and the Tamang but not in the Sylheti women may be related to the extreme and long-standing fluctuations in energy balance in the former three groups but not in the latter one. Additionally, a comparatively greater exposure to immune insults among the first three populations could also contribute to lower chronic levels of ovarian function. Unfortunately, there are no salivary oestradiol data in populations with more moderate energetic conditions against which to contrast the results for Sylheti women.

Although not entirely comparable, the lack of differences in salivary oestradiol levels between women in Bangladesh and those in the UK are also in contrast with findings of a clinical study in which Key and collaborators (1990) reported significantly lower plasma oestrogen levels in rural Chinese women compared to British women (Key et al., 1990). However, the discrepancy between the two studies may be due to contrasting methodologies and sampling protocols (a single plasma sample during the luteal phase vs. complete menstrual salivary profiles in our study).

Migrant studies and oestradiol levels

There are two other migrant studies of oestrogen levels where participants have been distinctly defined on the basis of their migration status rather than just their ethnic background. In contrast to our results, one investigation involving first generation college students of Indian and

Pakistani origin living in the USA did find significantly lower mid-follicular plasma oestradiol levels among migrants compared to white Americans, as well as a positive association between length of time in the USA and steroids levels. The effect of age at migration was not discussed (Kamath *et al.*, 1999).

On the other hand, our results agree with a second migrant study aimed at evaluating how lifestyle differences affect endogenous oestradiol concentrations and breast cancer risk (Falk *et al.*, 2002). In this study, pre-menopausal women of southeast Asian descent living in the USA were classified according to a migration history index (a composite of the subject's place of birth, usual residence in Asia (urban/rural), length of time living in the West, and grandparents' place of birth). Despite important differences in methodology (e.g. single mid-luteal plasma samples) and study design (e.g., no available information on age at migration), and the fact that migrants were from a wide range of countries of varied standards of living (Japan, China, Philippines and Hawaii), the results were very similar to those obtained in the present study for Bangladeshi migrants to the UK. Falk *et al.* found that plasma levels of oestrogen and sex hormone-binding globulin (SHBG) did not differ significantly between Asian- and Western-born women. As was the case for our data, results did not change even after adjusting for anthropometric and reproductive variables, nor was there a significant positive trend in oestrogen levels with migration history. Although the least "Westernised" group tended to record lower (but not significantly so) oestrogen levels, it is unclear whether this was related to place and/or country of birth, length of exposure in the USA or age at migration. The lack of precision on the migrants' origin limits any conclusions as to how extreme the changes in environment after migration were for each of the groups studied, and how these compare to the changes experienced by Bangladeshis moving into the UK. Migrants from Japan and Hawaii probably had less of a radical experience than those from China or the Philippines, but without detailed

migration histories, any potential differences remain speculative. The study did not include groups of women still living in the countries from which the groups of migrants originated, which prevents any evaluation of whether or not oestradiol levels change upon migration relative to baseline levels in the country of origin.

In conclusion, the evidence available in the literature for the effect of migration on oestradiol levels is scarce and inconsistent. The diversity of methodologies, sampling protocols and populations may account for the variance observed. None of the previous studies included comparisons with groups from the countries of origin, which prevents any assessment of changes in oestradiol levels upon migration. The lack of detailed information on age at migration and the magnitude of the change in conditions between the host country and the country of origin also hinder interpretation of these data in the context of a developmental hypothesis.

Developmental hypothesis: oestradiol levels

The results of the present study for oestradiol fail to support the predictions of the developmental hypothesis, because: a) groups who developed in a poor environment (Bangladesh) do not have significantly lower oestradiol levels than those who developed under more affluent conditions in the UK; and b) women who moved from Bangladesh to the UK while growth was ongoing do not show higher oestradiol levels than those who remained and matured in Sylhet. In other words, no evidence was found of a significant developmental effect on oestradiol levels.

It is possible that by using cycle regularity and average menstrual length (25-35 days) as eligibility criteria in this study, the sample was inadvertently biased towards women with "more robust" ovarian function in all groups and by implication, towards individuals in the upper range of their group distribution. Unfortunately, no data on the differential incidence of irregular cycles among groups is available to substantiate

this hypothesis. Moreover, the obvious question to follow is why the sampling procedure would have obscured any group differences in oestradiol levels but not for progesterone.

One explanation may relate to the different roles each steroid plays in determining menstrual characteristics. The role of oestradiol as the main steroid implicated in gamete maturation and development is well documented. Variation in the length of the menstrual cycle and, by implication, its regularity is largely due to variation in the length of the follicular phase which is negatively related to the quality and growth rate of the follicle, itself determined by oestradiol levels (Eissa et al., 1986; Apter et al., 1987; Fritz et al., 1987; Yoshimura & Wallach, 1987). Progesterone in turn, is positively associated with the length of the menstrual cycle through its action on the maintenance of the endometrial epithelium after ovulation (Maslar, 1988; Stouffer, 1988). Because the main effect of progesterone occurs in the second part of the cycle (luteal), it can be said that this steroid is tightly related to, but downstream from the action of oestradiol. The precedence of oestradiol over progesterone in the timing of the events of the menstrual cycle means that any selection criteria based on menstrual regularity is likely to blur variation mostly in oestradiol and not necessarily in progesterone. Given high enough oestradiol levels to maintain cycle regularity, progesterone levels can, within limits, remain low without noticeable changes in menstrual length (McNeely & Soules, 1988). According to the present study's eligibility criteria, those women whose luteal progesterone levels are abated to a point where menstrual regularity is compromised would have been left out of the sample. In this way, biased selection towards "robust" cycles is likely to have had a stronger impact on group differences in oestradiol levels rather than in progesterone, but still kept within-group variation in both hormones.

Another interpretation for the lack of evidence of a developmental effect on oestradiol levels is that developmental effects on progesterone are

somehow more pronounced than those for oestradiol (assuming that they do indeed exist). Alternatively, each steroid may be impacted in different ways by current environmental conditions. It is plausible that both hormones are indeed affected by long-term energetic conditions over formative periods, but that they differ with respect to how they respond to acute energetic changes; that is, how they vary about the set-points established during development.

Due to historical problems of establishing viable salivary oestradiol assays, most research on ovarian function until recently has focused on salivary progesterone. As a result, much less is known about how oestradiol responds to ecological and compositional variables, or how it compares to progesterone in all these respects. Nevertheless, the few studies where comprehensive salivary profiles for both hormones have been obtained throughout the menstrual cycle provide some evidence that the two steroids do somehow behave differently and sometimes contrast with each other. For example, Lipson and Ellison's (1996) study of conception and non-conception cycles in white women in the USA showed higher follicular oestradiol but not luteal progesterone levels in the conception cycles (Lipson & Ellison, 1996). Intra-individual comparisons also revealed a significantly positive correlation between relative body weight and mid-follicular oestradiol concentration, and hence with the probability of conception; no such significant correlation was found for progesterone. In other words, oestradiol and progesterone appear to differ in their sensitivity and in the way each responds to short-term changes in energetic conditions.

Further evidence for differences between progesterone and oestradiol comes from a comparison of rural Aymara women in Bolivia and UK white women, two groups living in greatly contrasting energetic conditions. Results show that progesterone levels in poor Aymara women are significantly lower than in their affluent white counterparts both in conception and non-conception cycles (Bentley *et al.*, 1998), and

throughout pregnancy (Vitzthum *et al.*, 2004). In contrast, oestradiol levels in Aymara women are significantly lower only in non-conception cycles; during conception cycles such differences disappear and the concentrations between whites and the Aymaras are comparable (Bentley *et al.*, 2000; Horton, 2003). Unfortunately, no data on the association between anthropometric variables and oestradiol levels have been presented for these groups. However, based on the results for USA women, it can be speculated that the variation in oestradiol levels between conception and non-conception cycles in the Aymara women is also related to short-term changes in energy balance. Given the pre-eminent role of oestradiol in determining the quality of the oocyte and, by implication, the chances of successful reproduction, the higher sensitivity of this hormone to acute energetic conditions compared to that of progesterone may be seen as part of the strategy to optimise reproductive effort and ultimately fitness. Another implication of the findings of the natural conception studies is that oestradiol profiles obtained over a single menstrual cycle are more likely to reflect the impact of current/recent energetic conditions than of chronic effects and hence are poor indicators of an individual's energetic history.

On this basis, it can be concluded that, while the oestradiol results of the present study do not support the predictions of the developmental hypothesis, they should not be taken as evidence to reject it outright either. In other words, the lack of significant differences among groups cannot be taken as failing to demonstrate an effect of chronic conditions on oestradiol levels, but rather, it may indicate that the current energetic conditions at the time of sampling were not dissimilar among the study groups and thus yielded comparable oestradiol levels.

It therefore remains plausible that groups who experience contrasting energetic conditions during growth differ with respect to reproductive characteristics relating to this steroid. These could include the proportion of "robust" cycles with high oestradiol (i.e. with good potential for

conception), the frequency of anovulatory cycles, and other qualitative characteristics such as ultradian patterns of expression. A longitudinal approach will be required to further evaluate the developmental hypothesis on oestradiol levels.

CHAPTER 6

Changing lifestyle and reproductive variables among generations of Bangladeshi migrants in London: implications for breast cancer risk

Breast cancer risk in the Bangladeshi community in the UK

There is a common perception reflected in the clinical literature that women of South Asian origin (Indians, Pakistanis, and Bangladeshis) are at low risk for breast cancer. This perception is supported by available cancer mortality and incidence data. For example, standardised mortality rates for South Asians in the UK are about half those of the general population (Barker & Barker, 1990; Balarajan & Raleigh, 1993; Wild & McKeigue, 1997; Acheson, 1998; Bhopal, 2002). Estimated age-standardised rates are also considerably lower than those of the native English population (46 per 100,000 vs. 73 per 100,000, respectively) (Winter *et al.*, 1999). In terms of risk factors, South Asians typically have dietary and reproductive patterns that are protective against breast cancer (McCormack *et al.*, 2004), namely a high parity, early age at first birth, a high prevalence of breastfeeding (OPCS, 1993; Thomas *et al.*, 1997a; ONS, 2004a), and a fibre-rich traditional diet (Smith *et al.*, 1993; dos Santos Silva *et al.*, 2002). However, recent evidence indicates that risk factors for migrants are changing. Consistent with patterns observed in other migrant populations (Shimizu *et al.*, 1991; Ziegler *et al.*, 1993), the breast cancer incidence in South Asian groups in the UK is moving in the direction of the host population and away from the low rates prevalent in the Indian Subcontinent. For example, age-standardised breast cancer rates for English South Asians (1990-1992) are almost double those reported in the 1983-1987 Bombay registry (Winter *et al.*, 1999; Smith *et al.*, 2003b).

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An evolutionary perspective on breast cancer among affluent developed countries may help us in understanding these kinds of transitions among migrant populations such as South Asians to the UK.

Evolutionary perspectives on Breast Cancer Risk

The evolutionary paradigm for the relationship between reproductive ecology and ovarian function provides a framework for understanding several aspects of reproductive cancer epidemiology, as well as global patterns of reproductive cancer incidence (Ellison, 1999).

Using this perspective, the current incidence patterns and risk profiles are thought to be the outcome of a departure from the ancestral developmental and reproductive parameters within which humans evolved (Eaton *et al.*, 1994; Ellison, 1999; Strassman, 1999; Greaves, 2000). Specifically, it proposes that human reproductive physiology evolved to function under conditions of acute and chronic energetic stress, and thus, when such constraints are removed, as in the case of contemporary privileged populations living in environments of energetic surplus, the sensitivity of the system to ecological cues turns maladaptive and leads to disease. Theoretical estimates show reproductive cancers risks 10-100 times greater among Western affluent women than in their pre-agricultural counterparts (Eaton *et al.*, 1994).

Reproductive ecologists have argued that such dramatic increases in cancer incidence moves in parallel with the secular trends in growth and maturation characteristic of economic development and industrial modernisation. They suggest that the numerous nutritional, health and lifestyle changes that follow these transformations, have led reproductive and developmental patterns in the direction of enhanced gonadal steroid production and increased lifetime exposure, both associated with a higher risk for reproductive cancers.

Epidemiological data show that the highest incidence of such cancers is generally found among privileged populations that grow faster, mature earlier, have higher average caloric intakes and lower average energy expenditures (Henderson & Bernstein, 1991), all factors associated with high levels of gonadal function (see Table 12). Rural/urban populations at different stages of this secular trend also exhibit differential incidence of reproductive cancers (Rimpella & Pukkala, 1982). Similarly, the accelerated transition to high risk seen in many migrant populations that have come from settings of lower cancer incidence is in the same way related to the accelerated secular trend in such groups (Trichopolous *et al.*, 1984; Thomas & Karagas, 1987; Shimizu *et al.*, 1991; Ziegler *et al.*, 1993).

Along with the changes in constitutional variables brought about by rising living standards and general health of populations in transition, there are important changes in behaviour in response to and as a consequence of socio-economic transformations. Such behavioural adjustments also have the potential to impact cancer risk by affecting lifetime exposure to ovarian steroids. For example, a late age at first reproduction, low parity and low incidence and duration of lactation common to higher socio-economic groups of developed countries are associated with a lower lifetime risk for breast cancer (Henderson & Bernstein, 1991; Kelsey *et al.*, 1993).

In sum, from the perspective of reproductive ecology, the high steroid levels and consequently elevated risks of reproductive cancers are additional manifestations of the accelerated growth and maturation and modified reproductive behaviours characteristic of recent human history. The prediction is that as populations develop and traverse through a secular trend in growth and maturation, the incidence of these malignancies will rise.

The present study presents an opportunity to explore, albeit at a small scale, some of the social and biological transformations associated with migration among Bangladeshis in London. In this section, the hormonal findings, together with data on behavioural variables reconstructed from the questionnaires, will be used to illustrate how lifestyle and reproductive risk factors for breast cancer may be changing between migrant generations, as well as how they compare to the sedentee and the host population.

The purpose of this analysis is not intended as the basis for advancing epidemiological predictions regarding risk factors profiles for Bangladeshis in the UK, for it is understood that the sample from which its drawn is not representative of the population at large. Nor is it intended as an exhaustive review of the factors that affect breast cancer epidemiology. Rather, the aim is to profit from the rather detailed information on individual reproductive and lifestyle histories of women of different generations to sketch possible trends in this community. The value of this exercise is that, to my knowledge, it is the only available data set for this ethnic group in the UK that purposely distinguishes between individuals on the basis of their country of birth (1st vs 2nd generation), and age at migration. This allows for finer descriptive analysis than is possible in other available surveys, where migrant status is confounded with ethnicity (OPCS, 1993; Hirani & Primatesta, 2001; ONS, 2004a). This modest description may serve as a starting point for further investigations.

Following the example of similar exercises (Eaton *et al.*, 1994; Ellison, 1999; Strassman, 1999; Greaves, 2000), the analysis will follow the model developed in the context of reproductive ecology, where female ovarian function serves as a common pathway through which many categories of risk for breast cancer affect the initial appearance and subsequent growth of cancerous tissue and, ultimately, clinical incidence (Ellison, 1999). It will focus on comparing developmental, reproductive,

energetic and nutrition variables that have already been identified as established risk factors for breast cancer through their association with increased acute, chronic and cumulative exposure to endogenous ovarian steroids, progesterone and oestradiol (Kelsey *et al.*, 1993; Henderson *et al.*, 1996; Bernstein, 2002). Attention will be paid to developmental characteristics which may also be particularly important for certain of these risk factors, such as stature and early menarche, since these characteristics, as demonstrated in the present study, can be used as markers of high set-points for adult gonadal function.

The following is a list of the risk factors analysed:

1. Specific levels of reproductive ovarian steroids during each cycle.

2. Reproductive variables that impact the lifetime cumulative exposure of breast tissue to reproductive steroids:

      a) Age at menarche

      b) Age at menopause

      c) Age at first full term birth

      d) Parity

      e) Lactational practices

3. Non-reproductive variables that affect the levels of circulating steroids and/or menstrual regularity:

      f) Obesity and weight gain

      g) Diet

      h) Levels of physical activity

4. Height

1. Actual levels of reproductive steroids

A large body of data connects high levels of oestradiol typical of affluent Western populations with an increased risk of breast cancer (e.g., (Bernstein & Ross, 1993; Pike *et al.*, 1993; Thomas *et al.*, 1997b; Key, 1999; Yu *et al.*, 2003). In this study, however, no significant differences were found in oestradiol levels between Bangladeshi migrants, Sylheti sedentees or white women (total cycle oestradiol $\bar{X}$ = 11.0 ± 0.9 pg/ml for Sylhetis; $\bar{X}$ = 12.4 ± 0.9 pg/ml for adult migrants; $\bar{X}$ = 10.4 ± 1.2 pg/ml for child migrants; $\bar{X}$ = 9.0 ± 1.1 pg/ml for second generation women, $\bar{X}$ = 10.8 ± 1.0 pg/ml for white women). If these data derived from a single cycle are indeed representative of average chronic oestradiol levels, then differences in risk between generations due only to the *actual* levels of this ovarian hormone would not then be expected (see Chapter 5 for a detailed discussion of the hormonal data). In contrast, levels of progesterone among migrants who grew up in England were found to rise significantly (luteal progesterone $\bar{X}$ = 38.9 ± 5.7 pg/ml for child migrants; $\bar{X}$ = 40.1 ± 5.5 pg/ml for second generation women) compared to women who grew up in Bangladesh ($\bar{X}$ = 24.6 ± 2.5 pg/ml for adult migrants; $\bar{X}$ = 22.2 ± 3.0 pg/ml for Sylheti sedentees). Moreover, in only one generation, progesterone concentrations reached levels indistinguishable from those of the white UK group ($\bar{X}$ = 45.1 ± 4.3 pg/ml).

The epidemiological evidence for an association between high levels of progesterone and a high risk of breast cancer is more scant and inconsistent compared to oestradiol, possibly due to methodological issues; specifically, the need to synchronise the sample collection to mid-luteal phase of ovulatory cycles, when progesterone is highest (Bernstein & Ross, 1993). However, there are correlational data that point to a strong positive relationship between average progesterone values at a population level and breast cancer incidence rates (Jasienska & Thune, 2001). Based on this and the available

experimental data on the role of progesterone in breast cancer development (Henderson *et al.*, 1982; van Leeuwen, 1991; Stanford & Thomas, 1993; Gregoraszczuk. E *et al.*, 2001; ESHRE, 2004; Milewicz *et al.*, 2005; Wood & Hrushesky, 2005), it may be speculated that the significant change in chronic progesterone levels between Bangladeshi immigrant generations may increase the risk for this disease, especially among UK-born Bangladeshis.

2. Reproductive variables that impact the lifetime cumulative exposure of breast tissue to steroids:

a) Age at menarche

Age at menarche is an established risk factor for breast cancer, independent of other factors, including parity, age at first birth, and age at menopause. Younger ages at menarche are associated with modest elevations in breast cancer risk (Henderson *et al.*, 1981; Hsieh *et al.*, 1990; Kelsey *et al.*, 1993). Age at menarche affects cancer risk in three ways: 1) it marks the onset of menstrual cycles and, thus, the start of cyclical exposure of the breast tissue to ovarian steroids; 2) it determines the extent of the adolescent sub-fecund period which precedes the establishment of regular ovulatory cycles (early menarche is associated with a faster attainment of regular ovulatory cycles (Apter & Vihko, 1983); and 3) it influences levels of hormones themselves -- early menarche is associated with significantly higher oestradiol levels during the adolescent period and into adulthood (Vihko & Apter, 1984; Apter *et al.*, 1989).

This study found that there are significant differences in the self-reported age at menarche between the groups studied (Table 29). Child migrants reached menarche at an earlier age ($\overline{x}$ = 12.2 ± 0.2 yr) than either Sylheti sedentees ($\overline{x}$ = 13.2 ± 0.2 yr), adult migrants ($\overline{x}$ = 13.0 ± 0.2 yr), or white women ($\overline{x}$ = 13.1 ± 0.2 yr), while second generation women ($\overline{x}$ = 12.2 ± 0.3 yr) reached menarche earlier than women in Sylhet. The

child migrants and second generation group also have the lowest range of values of all the study groups (8 yr vs. 10, 10 and 11, for adult migrants, white women and Sylhetis, respectively). For child migrants who arrived in England before the upper range of menarcheal age (16 yrs) for first-generation migrants in this study (see methods section in chapter 5 for justification), there was a significant positive correlation between age at migration and menarcheal age (r= 0.31, p=0.03) (Figure 9). Similarly, UK-born daughters of first and second generation women had a significantly younger age at menarche ($\bar{X}$ = 11.1 ± 0.3 yr) than daughters of Sylheti sedentees born in Bangladesh ($\bar{X}$ = 13.4 ± 0.2 yr), but there were no differences between these girls and the daughters of the white women ($\bar{X}$ = 12.4 ± 1.1 yr) (Table 29).

These results indicate that Bangladeshi women who were born and/or grew up in England tend to have an earlier menarcheal age than women who arrived as adults. This implies that the risk of breast cancer associated with this variable may be significantly different for women of different generations. Child migrants, as well as second and third generation women may potentially be at higher risk compared to those who migrated as adults. The significant positive correlation between age on arrival in the UK and menarcheal age, together with the evidence for higher progesterone levels among women who matured comparatively earlier in this study, could imply that women who migrated as young children are comparatively worse affected. This association adds a developmental component to the inter-generational differences in the impact of age at menarche as a risk factor for breast cancer.

b) Age at menopause

Epidemiological studies have consistently demonstrated that a late age at menopause is associated with a greater risk of breast cancer (Trichopolous et al., 1972). The rationale for this association is that a late

age at menopause represents a longer period of exposure to ovulatory menstrual cycles.

In this study, women were asked if they knew their mother's age at menopause. Given the second-hand and retrospective nature of these reported data, there is an unknown degree of recall bias, but the bias is likely to be similar, at least, across the groups (Table 29). (The calculation for mother's age at menopause includes only those women with an explicitly stated natural menopause, the rest were omitted from the analysis). The mothers of white women reached natural menopause at a significantly older age than mothers of Sylheti and migrant women (52.4 vs. 47.0 yr, 46.5 yr, 48.9 yr and 47.2 yr, for Sylheti, adult migrant, child migrant and second generation groups, respectively). Among Bangladeshi migrants, their mothers' age at natural menopause does not appear to differ from that of their Sylheti counterparts. However, lack of information on the country (and by implication, environmental conditions) in which the mothers of migrant women had lived and reached the menopause prevents any conclusions regarding trends among migrants.

There is sparse and indirect evidence that growth in early childhood may affect age at menopause, with poor growth rates associated with an earlier menopause (Parazzini et al., 1992; Van Noord et al., 1997; Hardy & Kuh, 1999). Inasmuch as the evidence is limited, it could be speculated that the older age at menopause among white women compared to their counterparts in Sylhet could be related to the better conditions in England, and that migrant populations should show a trend towards a later age at menopause as well. Such a trend has been observed in a study of Hispanic migrants in the USA that found second generation migrants reached the menopause at significantly later ages compared to first generation women (Leidy, 1998). If a similar pattern were to follow among Bangladeshis in England, subsequent generations would experience menopause at later ages and potentially be at comparatively higher risks for breast cancer.

Table 29. Menarche and participant's mother's menopause by group

			GROUP		
	SYL	ADU	CHI	2ndGEN	WHI
Self-reported age at menarche (yrs) (X ± SE; n) [a]					
mean	13.2	13.0	12.2	12.3	13.1
SE	0.2	0.2	0.2	0.3	0.2
n	44	40	50	31	46
range	11-16	10-15	8-16	8-16	10-17
Participant's daughter's age at menarche (for migrant groups only UK born daughters are included; closed cases only) [b] **(X ± SE; n)**					
	13.4 ± 0.2 (5)		11.1 ± 0.3 (20)		12.4 ± 1.1 (5)
range	13-14		8-13		11-14
Mother's age at menopause (closed cases only) [c] **(X ± SE; n)**	47.0 ± 1.2 (27)	46.5 ± 1.1 (14)	48.9 ± 1.4 (14)	47.2 ± 1.6 (20)	52.4 ± 0.9 (16)

[a] Calculation for mother's age at menopause include only those women with explicitly stated natural menopause, those with reported artificial menopause were not considered for the analysis.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] MENARCHE (CRITERIA <= 16 y (CHI)/ 17+(ADU): One-way ANOVA $F_{4,210}$=5.3 p<0.001; SYL>CHI p<0.001; > 2ndGEN p<0.05; ADU>CHI p=0.05; WHI>CHI p<0.01

[b] One-way ANOVA $F_{2,31}$=9.65 p<0.001; SYL > 3MIG p<0.001

[c] One-way ANOVA $F_{4,86}$=2.86 p<0.05; WHI > SYL p<0.05

c) Age at first birth

There is a linear increase in breast cancer risk with increasing age at first birth which is independent of other known factors (Kelsey *et al.*, 1993). It is thought that the protective effect of early age at first full pregnancy is mediated in two ways: 1) by driving final differentiation of the breast tissue and reducing the risk of further mutations; and 2) by permanently increasing the levels of sex hormone binding globulin (SHBG) and, thus, reducing the amount of circulating free oestrogens readily available to receptors in the breast tissue (Bernstein *et al.*, 1985).

A Kaplan-Meier survival function analysis found significant differences in *estimated* age at first birth between migrant groups, with significantly older ages at first birth for UK-born generations ($\bar{x}$ = 21.8 ± 0.5 for adult migrants; $\bar{x}$ = 24.5 ± 0.9 for child migrants; $\bar{x}$ = 26.6 ± 0.9 for second generation; logrank = 19.7, df = 2, p<0.001) (Table 30 and Figure 20). Similarly, significant differences were found in the period elapsed between menarche and first reproduction, with longer waiting times for UK-born women ($\bar{x}$ = 9.1 ± 0.5 for adult migrants; $\bar{x}$ = 12.7 ± 0.9 for child migrants; $\bar{x}$ = 13.6 ± 0.5 for second generation; logrank = 23.9, df = 2, p<0.001) (Table 30 and Figure 21). Additionally, there is evidence that marriage is being delayed among younger generations (Table 4) compared to older first generation women. This probably as a result of more women entering formal employment and having longer educational careers (see Chapter 2 - section marital status).

Although no data are available on contraceptive use, these results suggest inter-generational differences in reproduction decision-making which may affect breast cancer risk. With a decreasing age at menarche and a delay in the start of the reproductive career among younger generations of British-Bangladeshis, the lapse of uninterrupted menstrual cycles (in the absence of oral contraceptive use) could potentially put them at comparatively higher risk.

d) Parity

Pregnancy has a dual effect on breast cancer, involving a short-term increase in risk followed by a long-term protective effect (Bruzzi *et al.*, 1988). Pregnancy is associated with high levels of oestrogens, progesterone, and prolactin. These high hormone levels induce breast cell differentiation as well as cell proliferation, and this could explain the biphasic effect of pregnancy on breast cancer: pregnancy may be protective by reducing the pool of susceptible stem cells through differentiation, or conversely, promote breast cancer by inducing proliferation of cells that have already suffered malignant transformation (Bernstein *et al.*, 1985). Nevertheless, there is ample evidence for a protective effect of high parity on breast cancer independent of the effect of age at first birth (MacMahon *et al.*, 1970; Yuan *et al.*, 1988; Kelsey *et al.*, 1993; Albrektsen *et al.*, 1994).

All women in this study were of reproductive age (18-39); ($\overline{X}$ = 26.1 ± 0.6 for Sylheti; $\overline{X}$ = 31.8 ± 0.7 for adult migrants; $\overline{X}$ = 27.8 ± 0.6 child migrants; $\overline{X}$ = 24.4 ± 0.6 for second generation; $\overline{X}$ = 31.2 ± 0.7 for white women) but many had not yet begun childbearing; therefore, all figures reported here regarding average number of children of women reflect incomplete reproductive spans. In fact, only 29% of second generation, and 56% of child migrant women, included in this analysis were parous at the time of the study (vs. 82% of adult migrants, 25% of sylheti and 36% of white women). Therefore, it is probable that the final average number of children for each group will turn out to be larger than that reported here. Taking these limitations into account, the available data show that all migrant groups, including second generation women, exhibit, on average, higher fertility than their white counterparts and comparable levels to Sylheti sedentees (no. children $\overline{X}$ = 2.7± 1.6 for adult migrants; $\overline{X}$ = 2.5 ± 0.2 for child migrants; $\overline{X}$ = 2.4 ± 0.2 for second generation, $\overline{X}$ = 2.2 ± 0.3 for Sylheti sedentees, and $\overline{X}$ = 1.7 ± 0.2 for white women). Moreover, the proportion of women with 3 or more

children was approximately 50% in all three migrant groups (57%, 46% and 50% for adult migrants, child migrants and second generation women, respectively) compared to only 17% for white women (Table 30).

Small sample sizes and unfinished reproductive spans prevent too many generalisations, but these results show that reproductive patterns among first generation migrants in the UK may not differ considerably from those observed in the Sylheti sample, regardless of the effect of time since migration or age at migration. Population-based surveys have previously described the high fertility characteristic of first-generation Bangladeshis in the UK. Unfortunately, lack of appropriate data on migration status prevents inter-generational comparisons in such surveys (Summerfield & Babb, 2003).

Our data on socio-economic variables indicate that young British-Bangladeshi generations are in many respects moving away from the traditional customs of the older generations, but a high fertility rates appears to remain. Future work, when the second generation now at the beginning or half way their reproductive careers have completed their reproductive life-spans, will be able to clarify whether there are any significant differences in total fertility rate compared to the previous generation. This would determine whether younger generations of Bangladeshis continue to benefit from the protective effect of high fertility characteristic of the preceding generation.

Table 30. Reproductive statistics for all groups

			GROUP		
	SYL	ADU	CHI	2ndGEN	WHI
Estimated age at first full term birth[a] (X ± SE; n)	31.8 ± 1.2 (47)	21.8 ± 0.5 (58)	24.5 ± 0.9 (49)	26.6 ± 0.9 (35)	31.0 ± 1.4 (41)
range (closed cases)	16.5-26	17-30	17-29	16-25	18-29
Estimated no. years between menarche and first pregnancy[b] (X ± SE; n)	15.5 ± 0.8 (53)	9.1 ± 0.5 (57)	12.77 ± 0.9 (50)	13.6 ± 0.9 (33)	16.7 ± 1.5 (50)
range (closed cases)	2.5-15.5	3-17	2-15.2	4-13	1-20
Number of pregnancies [.] (X ± SE; n)	2.4 ± 0.3 (14)	3.0 ± 0.2 (54)	2.8 ± 0.2 (29)	2.5 ± 0.5 (10)	1.8 ± 0.2 (27)
range	1-4	1-7	1-6	1-5	1-6
median	2	3	3	2.5	2
Number of pregnancies by age [.] (X ± SE; n)					
18-25 y	1.7 ± 0.3 (3)	1.0 ± 0.0 (1)	3.0 ± 0.0 (1)	1.8 ± 0.4 (5)	2.0 ± 1.0 (2)
26-30 y	2.0 ± 0.4 (4)	2.8 ± 0.3 (13)	2.1 ± 0.2 (10)	3.2 ± 0.8 (4)	1.8 ± 0.6 (5)
31-35 y	3.2 ± 0.5 (4)	2.9 ± 0.3 (14)	2.7 ± 0.4 (11)	4.0 ± 0.0 (1)	1.3 ± 0.1 (10)
36-39 y	4.0 ± 0.0 (1)	3.7 ± 0.3 (19)	6.0 ± 0.0 (1)	..	2.1 ± 0.3 (7)
Interbirth interval (years) (all pregnancies) [.] (X ± SE; n)	3.0 ± 0.6 (19)	3.4 ± 0.2 (109)	3.0 ± 0.3 (51)	2.5 ± 0.6 (15)	3.4 ± 0.4 (23)
range	1-11	1-11	0-9	1-6	1-7
Interbirth interval (years) per woman (multiparous) [.]	2.8 ± 0.5 (11)	3.8 ± 0.3 (47)	3.3 ± 0.4 (26)	2.3 ± 0.4 (8)	3.5 ± 0.5 (15)
Number of live children [.] (X ± SE; n)	2.2 ± .3 (13)	2.7 ± 1.8 (53)	2.5 ± 0.2 (28)	2.4 ± 0.4 (10)	1.7 ± 0.2 (18)
range	1-4	1-5	1-5	1-5	1-3
No children (% parous women within groups)	(n=13)	(n=53)	(n=28)	(n=10)	(n=18)
1	23	17	14	40	50
2	46	28	39	10	33
3	15	36	32	30	17
4+	15	21	14	20	..

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] Kaplan-Meier Survival function- Age at first full time birth (Migrant groups only: censured and non-censured cases): df=2, logrank= 19.75, p=0.001

[b] Kaplan-Meier Survival function- Years elapsed from menarche to first full time birth (Migrant groups only; censured and non-censured cases): df=2, logrank= 23.89, p=0.001

[.] Unfinished reproductive span; No statistical analysis performed; Unadjusted descriptive statistics presented to give an overview of the reproductive variables.

Figure 20. Survival function for age at first birth by group (only migrant groups).
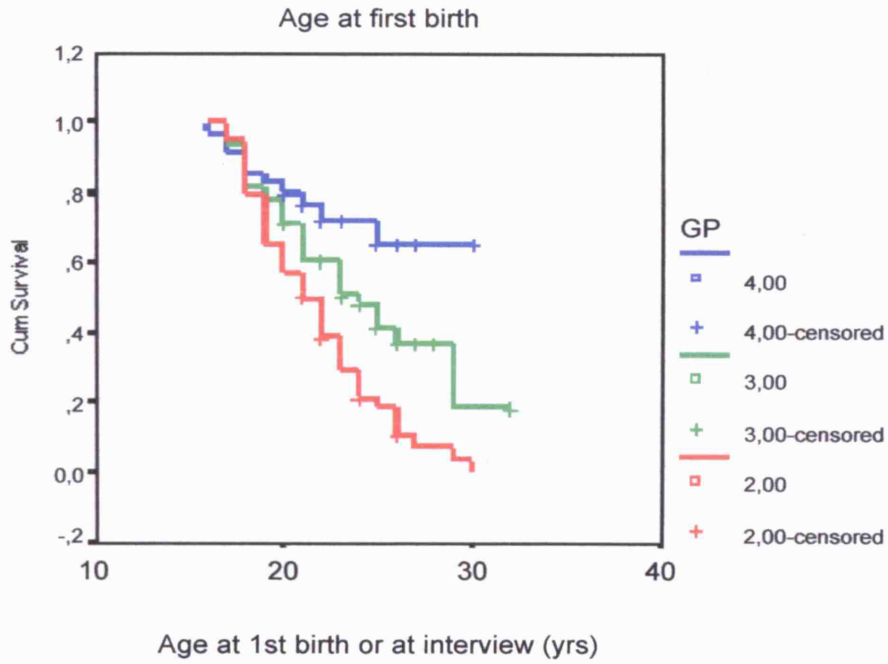
Age at first birth

Keplen-Meier Survival funciton- Age at first full time birth (Migrant groups only): df=2, logrank= 19.75, p=0.001

Figure 21. Survival function for number of years elapsed from menarche to first pregnancy by group (only migrant groups).

Time elapsed from menarche to 1st pregnancy
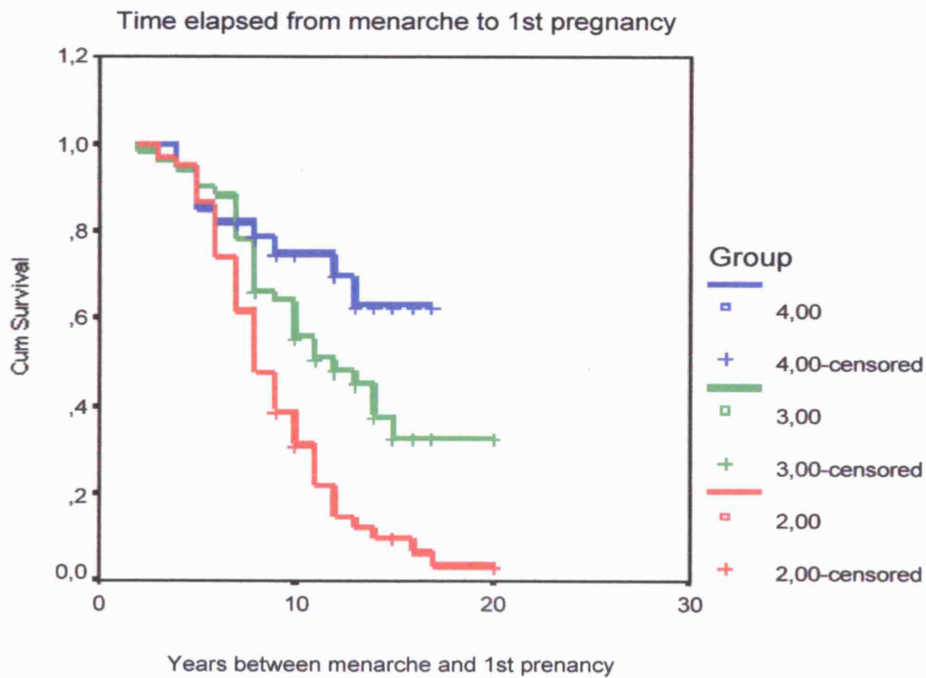
Keplen-Meier Survival function- Years from menarche to first full time birth (Migrant groups only): df=2, logrank= 23.89, p=0.001

e) Lactation

There is convincing evidence that lactation reduces the risk of breast cancer among women by suppressing ovarian function and reducing the lifetime cumulative exposure to ovarian hormones through periods of lactational amenorrhoea (Yuan *et al.*, 1988; Newcomb *et al.*, 1994; Enger *et al.*, 1997). This study shows that breastfeeding incidence, calculated as the proportion of babies who were ever breastfed, is highest for Sylheti babies (90%) and the Bangladesh-born offspring of adult migrants (100%). There were no significant differences in breastfeeding incidence between babies born in the UK to adult migrants (76%), child migrants (83%) and second generation women (83%). However, adult migrants were less likely to breastfeed children born in England (76%) compared to those born in Bangladesh (100%). White women had the lowest breastfeeding incidence of all groups (53%). Neither gender or birth order of the offspring had a significant effect on the incidence of breastfeeding in any of the groups (Table 31).

Duration of breastfeeding was measured as the length (in months) for which breastfeeding continued, regardless of when formula, solids, or other kinds of milk were introduced. Sylheti sedentees breastfed, on average, significantly longer than any other group ($\bar{x}$ = 16.2 ± 2.8 months). There were no differences in breastfeeding duration between the UK-born offspring of all three migrant groups and white women ($\bar{x}$ = 7.8 ± 0.8 months for adult migrants; $\bar{x}$ = 7.9 ± 1.1 months for child migrants; $\bar{x}$ = 4.8 ± 1.6 months for second generation women, and $\bar{x}$ = 6.2 ± 1.4 months for white women). However, adult migrants who gave birth in Bangladesh breastfed their offspring on average twice as long ($\bar{x}$ = 18.4 ± 2.2 months) than those who gave birth in the UK ($\bar{x}$ = 7.8 ± 0.8 months). Within subject comparisons show that Bangladesh-born children were breastfed on average 10 months longer than their UK-born siblings. Examination of data on individual subjects suggests that, overall, multiparous women were consistent in the length of time they

breastfed their various children. In general, long and short breast feeders remained so over their reproductive life.

Average differences in breastfeeding length between migrant groups living in the UK were not significant, but data on breastfeeding prevalence at different ages reveals contrasting patterns between groups. Breastfeeding prevalence was taken as the proportion of all babies who were wholly or partially breastfed at specific ages. For example, long breastfeeding was common among Sylheti women, with just under half (41%) continuing to breastfeed for over 15 months. The proportion of women who breastfed for over 15 months halved among first generation migrants in London, (23% and 22% for adult and child migrants, respectively), and decreased even more among second generation (6%) and white women (8%).

Number of years of education had no effect on breastfeeding incidence among Sylheti or Bangladeshi migrant groups but, in the white group, breastfeeding incidence was higher for women with more years of education. Mother's age had no effect on breastfeeding incidence among primiparous women in any of the groups.

The results of this study, although limited due to small sample sizes, argue for an important modification in breastfeeding patterns among Bangladeshi migrants in the UK. The variables implicated in such changes are likely to be many and varied in nature and probably relate to changes in family structure and lifestyle that have resulted from adapting to a different socio-economic system and culture (see Chapter 2 for a detailed analysis). As discussed earlier, such changes have been particularly radical for females. Many first, and most second generation women have acquired extra roles in addition to traditional ones. Time and energy have to be allocated between activities outside the home and domestic ones. With an increasing number of women in employment, many of them providing a large proportion of the family

income, constraints typically associated with a decreasing incidence and shorter duration of breastfeeding have emerged for the Bangladeshi community. The disappearance of the extended family also has meant that housework and childcare are no longer shared with other female members but, instead, become the responsibility of a single woman. Given the fact that most British-Bangladeshi families are at the lower end of the economic spectrum, paid childcare or extended unpaid maternity leaves that might contribute to an increase in breastfeeding duration in this community are not realistic options.

Another factor associated with the economic disadvantage prevalent in most Bangladeshi households is overcrowding. The lack of privacy associated with high household densities was often mentioned by women as an important deterrent to breastfeeding. Exposure to the host culture through everyday life and the media may also contribute to a modification of feeding choices, since there is a striking difference in breastfeeding behaviour of adult migrant women depending on the country where they gave birth. The same women breastfeeding in different environments show radically different patterns more consistent with the prevailing ones in the country in question.

Overall, these results suggest that changes related to the experience of migration have had an impact on breastfeeding behaviour, most notably in the second generation group. The most apparent change is not in the overall incidence, but more in the reduction in average duration and prevalence of breastfeeding among British-born Bangladeshi women. In terms of breast cancer risk, the protective effect of long durations of breastfeeding and the suppression of ovarian function are likely to be undermined among young generations of women.

Table 31. Breastfeeding incidence, duration and prevalence

			GROUP		
	SYL	ADU	CHI	2ndGEN	WHI
Breastfeeding incidence by country of child's birth (% of all live births) [a]					
Bangladesh	90	100	83	83	..
UK [e]	..	76			53
Breastfeeding length (months) by country of birth (all ever breastfed births) [b,e]					
Bangladesh	16.2 ± 2.8 (27)	18.4 ± 2.2 (14)			
range	1-60	6-30			
UK	..	7.8 ± 0.8 (98)	7.9 ± 1.1 (58)	4.8 ± 1.8 (15)	6.2 ± 1.4 (18)
range	..	0.5-30	0.25-30	0.25-24	0.25-24
Total breastfeeding length [c]	..	9.1 ± 0.8 (112)			
range	..	0.5-30			
Average breastfeeding length (months) per woman (multiparous women only) [d]	17.5 ± 0.4 (11)	7.3 ± 1.1 (45)	6.6 ± 1.5 (25)	4.3 ± 0.8 (5)	2.9 ± 1.2 (14)
Prevalence of breastfeeding at different ages (all ever breastfed children) [**]					
% of women still breastfeeding at	(n=27)	(n=112)	(n=58)	(n=15)	(n=16)
> 1 week - 1 month	93	91	75	60	88
> 1 month - 4 months	89	53	56	33	76
> 4 months - 6 months	74	43	39	28	14
> 9 months - 12 months	48	24	22	6	8
> 15 months	41	23	22	6	8

[a] Incidence of breastfeeding refers to the proportion of children who were ever breastfed. Duration of breastfeeding refers to the length for which breastfeeding continued at all, regardless of when other milk and foods were introduced.

[**] prevalence of breastfeeding refers to the proportion of all children who were wholly or partially breastfed at specific ages.

Sample sizes are SYL(54), ADU(62), CHI (51), 2ndGEN (34) and WHI (50) unless otherwise stated.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[a] (UK only) Chi-square p<0.05

[b] (ADU only) T-test =22.51 p<0.001

[c] One-way ANOVA $F_{4,215}$=5.42 p<0.001; SYL> ADU, WHI p<0.01, > CHI, 2ndGEN p<0.05

[d] One-way ANOVA $F_{4,95}$=5.54 p<0.001; SYL> ADU, CHI p<0.01, 2ndGEN p<0.05, WHI p<0.001

3. Non-reproductive variables that affect the levels of circulating steroids and/or menstrual regularity:

f) Obesity and weight gain

Two aspects of the body mass index -- obesity and weight gain as an adult -- are associated with a higher breast cancer risk among postmenopausal women (Hunter & Willett, 1993). The increased risk in heavy postmenopausal women can be attributed to higher levels of circulating oestrogen in these women, since the main source of endogenous oestrogen after the menopause is the conversion of the androgen precursor androstenedione to oestrone in adipose tissue. Obesity is also related to reduced levels of SHBG and, therefore, to a higher tissue availability of oestrogens (Bernstein, 2002).

Results suggest a high prevalence of overweight and obesity among Bangladeshi migrants of reproductive age (Table 32 & Figure 22). Overweight rates (BMI $\geq$ 26 to < 30) were 36%, 20% and 31% for adult migrants, child migrants and second generation women, respectively, in contrast to 13% for Sylheti sedentees and 11% for white women. The overall rates for obesity (BMI $\geq$ 30) were 24%, 27% and 23% for child migrants, adult migrants and second generation women, respectively, compared to 3% for Sylheti sedentees and 11% for white women. The figures for all three migrant groups are considerably higher than those reported for females of the general UK population in equivalent age groups (likely as a result of small sample size) (DoH, 2002).

In contrast to the white and Sylheti groups, obesity is fairly prevalent both among very young women and among the oldest age category in the migrant groups. For example, in the youngest age group (18-29) 33% of child migrants and 50% of second generation women had a BMI $\geq$ 26 compared to 14% of white and 5% of Sylheti women. No data were available for adult migrants in this age group. In the age group closer to menopause (36+), 77% of adult migrants, and 100% of child migrants

had a BMI ≥ 26 compared to 29% of white women. No data were available for second generation women in this age group.

Among migrant groups, there was a strong effect of parity on BMI with parous women more likely to be overweight than non-parous ones (Table 18 & Table 32). In all migrant groups, the highest proportion of parous women was at least one BMI category higher than their non-parous counterparts. In contrast to adult migrant women -- among whom there were no overweight non-parous women -- 25% of child migrants and 45% of second generation women were already overweight before childbearing. The high incidence of overweight and obesity among young non-parous child migrants and second generation women compared to their white counterparts, together with the very low prevalence of these problems among Sylheti women of the same age group, may be taken as evidence of detrimental changes in lifestyle taking place among Bangladeshis growing up in the UK. A more Western lifestyle may be partly responsible for these changes where modification of dietary patterns and a more sedentary lifestyle may partly account for these trends. It is also plausible that the high prevalence of obesity in this group is an illustration of the thrifty phenotype phenomenon common among groups in economic transition whether migrant or not (Yudkin, 1996; Hales & Barker, 2001; Adair & Prentice, 2004). The high prevalence of diabetes and cardiovascular diseases reported for Bangladeshis living in the UK (McKeigue et al., 1988; Erens et al., 2001) may support this hypothesis.

The data presented here suggest that some aspects related to the migration experience have affected first and second generation women in similar ways with respect to changes in BMI. If the weight trends for pre-menopausal women in this study were to continue into later ages, a large proportion of first and second generation Bangladeshi women will be likely to enter the menopause with a high BMI. This could translate

into potentially higher risk for post-menopausal breast cancer for women in all three migrant groups.

Figure 22. Percentage of women in each BMI category by group (parous and non-parous women)

196
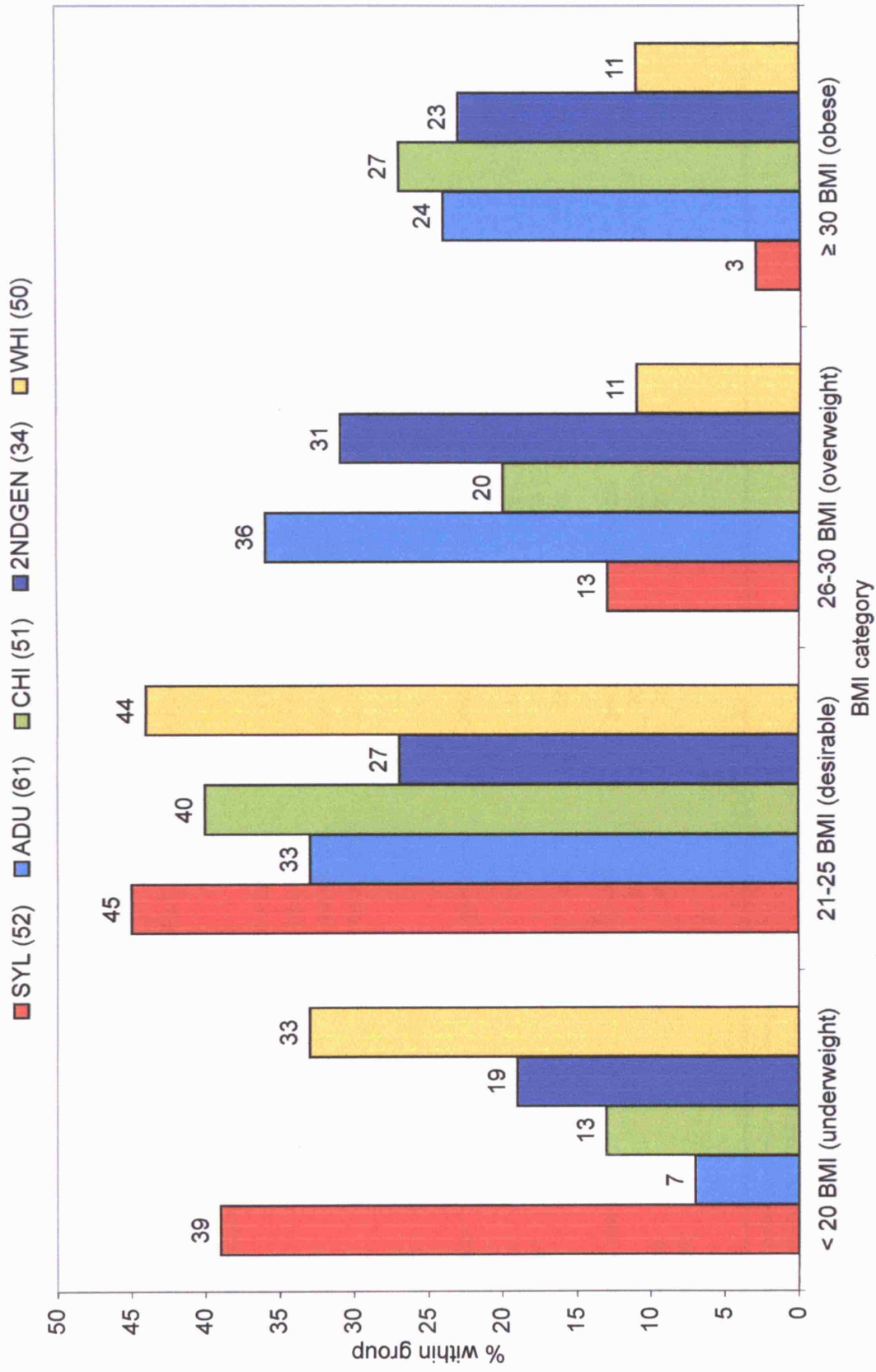
Table 32. Height and BMI data by group

	GROUP				
	SYL	ADU	CHI	2ndGEN	WHI
Height (cm) [*] (X ± SE; n)	153.2 ± 0.8 (52)	152.5 ± 0.5 (61)	154.2 ± 0.7 (51)	155.2 ± 0.9 (34)	163.9 ± 1.0 (50)
range	143.4-165.4	144.2-162.5	143.4-167.5	144.2-167.0	143.3-179.2
BMI (kg/m²) [*][b] (X ± SE; n)	22.6 ± 0.6 (52)	26.4 ± 0.5 (61)	25.6 ± 0.7 (51)	25.1 ± 0.9 (34)	23.4 ± 0.7 (49)
BMI (kg/m²) by age [ª] (X ± SE; n)					
18-25 y	21.8 ± 0.8 (28)	22.5 ± 1.2 (9)	24.2 ± 1.5 (16)	25.2 ± 1.1 (23)	21.2 ± 1.0 (8)
26-30 y	21.3 ± 0.8 (14)	25.2 ± 0.8 (16)	26.5 ± 1.1 (18)	24.5 ± 1.6 (10)	22.0 ± 1.1 (13)
31-35 y	25.0 ± 1.4 (8)	27.5 ± 1.1 (16)	25.5 ± 1.3 (15)	26.8 ± 0.0 (1)	22.9 ± 1.1 (15)
36-39 y	33.4 ± 2.1 (2)	28.3 ± 0.8 (20)	31.5 ± 0.0 (1)	..	26.5 ± 1.8 (13)
BMI (kg/m²) [*] (% prevalence within group)					
Parous women	(n=13)	(n=53)	(n=28)	(n=10)	(n=18)
BMI <= 20	18	..	6	..	50
21 <BMI >25	45	35	33	25	40
26 <BMI >30	27	40	28	62	..
BMI >=30	9	25	33	12	10
Non-parous women	(n=39)	(n=8)	(n=23)	(n=25)	(n=32)
BMI <= 20	48	75	25	28	27
21 <BMI >25	44	25	50	28	46
26 <BMI >30	7	..	8	17	15
BMI >=30	..	..	17	28	11

[*] Average values before correcting for age and parity.
[ª] Average values before correcting for parity.

Significance levels for pairwise comparisons are Bonferroni- adjusted.

[ª] HEIGHT: One-way ANOVA $F_{4,244}=36.82$ $p<0.001$; WHI >all groups $p<0.001$
[b] BMI: GLM $F_{10,213}=6.6$ $p<0.01$; age $F_{1,213}=9.7$ $p<0.01$; group $F_{4,123}=4.4$ $p<0.01$; parity $F_{1,213}=3.4$ ns; group*parity $F_{4,213}=2.3$ ns

g) Diet

Epidemiological studies have produced rather inconsistent and inconclusive results concerning the role of a high dietary fat intake and the risk of breast cancer (Hunter & Willet, 1996; Willett, 2001; dos Santos Silva *et al.*, 2002). However, there are data from the literature on dietary quality and steroid metabolism that point to a suppressive effect of low-fat/high-fibre diets on steroid hormone levels (Goldin *et al.*, 1982; Goldin *et al.*, 1986; Rose *et al.*, 1986; Longcope, 1990; Rose *et al.*, 1991; Goldin *et al.*, 1994; Bagga *et al.*, 1995; Boyd *et al.*, 1997; Rose *et al.*, 1997; Dorgan *et al.*, 2003). These studies suggest that a low fat/high fibre diet could potentially contribute to a reduced breast cancer risk. However, it has been suggested that breast cancer risk may be affected, not so much through a high dietary fat intake *per se*, but rather through the effects of this on body weight and composition. Thus, healthy dietary habits over the life course can be thought of as protective in that they lead to a stable and desirable body weight.

The traditional Bangladeshi diet consists of rice as a staple, pulses, and -- in the case of Sylhetis -- many varieties of fish, and to a lesser extent, lamb. Although the consumption of vegetables is relatively high, they are rarely eaten raw but rather coked in oil (*bhaji*), deep-fried or curried. Raw leafy vegetables and fruits other than those in season are rarely consumed. Dairy products are not prominent in the diet except as yoghurt and sweetmeats on special occasions (Kassam-Khamis *et al.*, 1995, 1996, 2000; Zannath & Edholm, 2004). Most Sylhetis are non-vegetarians and, as Muslims, the only dietary restriction is against pig meats. Overall, the traditional Bangladeshi diet could be regarded as relatively healthy on the basis of its high fibre, non-starch polysaccharides (NSP), and omega fatty acid content (dos Santos Silva *et al.*, 2002).

In general, despite the challenges of adjusting to a radically new lifestyle after migration, results from the diet questionnaire show that food habits

among migrant Bangladeshis in London, particularly first generation migrants, are similar to those prevalent in Bangladesh. However, the second generation already shows signs of a more Westernised diet as well as different eating habits. The data suggest that, with more women attending higher education and joining the workforce, family routines and time budgets are changing and with them the structure and character of family meals (qualitative data not shown). The need for convenient, time saving alternatives to the time-consuming traditional multi-courses meals is reflected in the higher consumption of convenient tinned and frozen meals. There is evidence of Western foods that are calorically dense and nutritionally poor in quality being steadily introduced into the diet, often under the influence of young, more acculturated children who are attracted to fast foods and ready meals. Similarly, there is a trend across generations, especially among younger women, to eat out. Student and employees reported eating lunch regularly at fast food places, which serve *halal* dishes.

Another practice taking root among the younger generations (especially child migrants and second generation women) is an increased consumption of sodas instead of plain water during mealtimes. In addition to sugary drinks, a higher consumption of processed foods as well as sweets and chocolates among these groups contributes to a higher intake of carbohydrates and salt. These dietary trends may partly account for the increased prevalence of obesity among young migrants discussed in the previous section.

With regard to the specific ingredients in the traditional diet, our data show evidence of a lower intake of pulses, fresh fruits and vegetables among child and second generation migrants, as well as a significant reduction in fish intake, particularly among the latter. Instead, possibly as a result of their improved economic situation, second generation women are eating red meat (lamb) much more frequently than their first-generation counterparts. Along with these unfavourable changes, there

are some in a healthier direction. For example, the younger generations (child migrants and second generation women) are eating more brown and wholemeal bread, preparing less fried food, and drinking less full-fat milk than the adult migrant groups.

In summary, the results in the present study show that the traditional Bangladeshi diet, which is high in complex carbohydrates and non-saturated fatty acids from pulses, vegetables and fish, is shifting towards one rich in energy-dense foods among younger generations. These changes in quality not only undermine the protective characteristics of the diet itself, but could also contribute directly to an increased risk of breast cancer through their damaging effects on body weight.

h) Levels of physical activity

There is evidence for a reduced risk of breast cancer associated with lifetime physical activity in pre- and postmenopausal women (Friedenreich & Rohan, 1995; McTiernan *et al.*, 1998; McTiernan, 2000). Physical activity is considered as a factor in breast cancer risk because of its potential effect on: 1) delaying age at menarche (Kelsey *et al.*, 1993; Bernstein, 2002) 2) ovarian function by suppressing ovulation and reducing circulating steroid levels (Russell *et al.*, 1984; Shangold, 1985; Ellison & Lager, 1986; Bernstein *et al.*, 1987; Howlett, 1987; Broocks *et al.*, 1990; Jasienska & Ellison, 1998; Jasienska *et al.*, 2000, 2004 (IN PREP)); and 3) lowering the BMI and preventing weight gain.

For most Bangladeshi women, household work and walking represent the only type of physical activity they undertake. Results from the lifestyle questionnaire show that, among younger generations, walking as an activity is decreasing. For example, while 87% of adult migrants reported walking daily for more than 20 minutes, only 59% of second generation women did so. This reduction in walking appears to be accompanied by an increase in driving among second generation women (17% vs. 7% and 12% in adult and child migrant groups,

respectively). In terms of household work, Bangladeshi women tend to assume all the responsibility for household chores, and unless second generation households become able to afford household help, levels of this activity among different generations are unlikely to change.

Given the poor tradition of physical exercise and sports activities among Muslim women, it is unlikely that Bangladeshi migrants would be able to take advantage of the protective effects of a lifetime of intense exercise. However, based on observations and informal conversations during recruitment, it could be argued that women will be more likely to get involved in sport and exercise activities, as younger generations of Bangladeshis become more exposed to Western perceptions of fitness and body image. In neighbourhoods with a high Bangladeshi population, there are already community and sport centres that cater for Muslim women and offer female-only swimming and exercise classes. These discrete changes may, in the long-term, increase physical activity levels among British-Bangladeshi women, and potentially contribute to lowering the prevalence of high BMIs, which in turn may translate in reduced cancer risk.

4. Compositional risk factors

i) Height

Height has been found to be positively associated with cancer risk independently of age at menarche and reproductive history (Howe *et al.*, 1990; De Stavola *et al.*, 1993; Kelsey *et al.*, 1993; Hunter & Willet, 1996; Swanson *et al.*, 1996; Okasha *et al.*, 2002, 2003). It is unclear by what mechanism height acts as a risk factor, but from a developmental perspective, it may be hypothesised that height is a gauge of nutritional and immunological factors during growth in early life, and thus an indicator of an endocrine blueprint that affects the susceptibility to breast cancer, specifically, a marker of high set-points for adult gonadal

function (Ellison, 1999). There is epidemiological evidence to support this idea: women who grow faster in childhood and reach an adult height above the average for their menarcheal category are at particularly increased risk of this malignancy (De Stavola *et al.*, 2004).

A secular trend towards increased height is a common feature of migrant populations following improvements in socio-economic conditions (Tanner, 1992; Roberts, 1994; Hauspie *et al.*, 1997; Cole, 2000). In this study however, average stature of second-generation women, although slightly higher ($\bar{X}$ = 155.2 ± 0.9 cm) than that of first-generation groups ($\bar{X}$ = 152.5 ± 0.3 cm for adult migrants; $\bar{X}$ = 154.2 ± 0.7 cm for child migrants) was not significantly different (Table 32). Nevertheless, the effect of migration on growth was observed in differences in height among women who arrived in England at different stages of development. Women who arrived in early infancy (0-2 years) are significantly taller ($\bar{X}$ = 159.8 ± 1.8 cm) than those who migrated at later ages ($\bar{X}$ = 154.0 ± 1.0 cm for arrivals at 3-8 years old; $\bar{X}$ = 152.8 ± 1.0 cm for arrivals ≥ 9 years) ($F_{=2,50}$ = 5.7, p = 0.1), which suggests that conditions associated to the UK environment have a positive impact on growth during early life.

With regard to the notion that high stature may be a marker of high set-points of ovarian function, the positive correlation observed between luteal progesterone and height in this study (r = 0.20, p = 0.004) was not significant when controlling for group (r = 0.05, p = 0.6) (Figure 6 & Table 14). Height was also found to be a non-significant determinant for luteal progesterone levels in multiple regression analyses. None of the oestradiol indices was significantly associated with height (Figure 7 & Table 14).

The results for inter-generational differences in height among migrant women in this study are suggestive but inconclusive, and no evidence of an association of high stature with higher levels of ovarian function was

found. Thus, by themselves, these data do not support the idea of potential higher breast cancer risk among younger generations as a result of improved linear growth. However, the significant trend towards earlier maturation among migrant Bangladeshi women who grew up in UK environments described earlier, would indicate that there is indeed an effect of migration on development. It is generally considered that improved growth and earlier maturation are interrelated characteristics of a secular trend. Although there are no longitudinal data available specifically for the Bangladeshis in the UK to this respect, it is hard to imagine that the trends in this community would be any different to other populations in transition. In this case, then, a concomitant increase in breast cancer risk would be expected.

5. Implications for public health

The inter-generational changes in the reproductive and lifestyle factors related to breast cancer risk described here, point on the whole, in the direction of increased risk for this malignancy for younger migrant generations. Albeit analysed on a very small scale, such trends are in line with patterns observed in other populations in transition (Henderson & Bernstein, 1991), and are known to accompany changes in disease incidence.

For South Asian women (which includes Indians, Pakistanis and Bangladeshis) in the UK, there are a series of epidemiological studies that already document the transition in incidence profiles.

For example, a recent study found that breast cancer rates among South Asians have increased over the last 10 years while having dropped among the rest of the population. In Leicester, a city with a large South Asian presence, the incidence ratios between 1990-1999, adjusted for age and deprivation tertile, were 1.37 in South Asian vs. 0.81 in non-Asian women (Smith et al., 2003b). Moreover, there is evidence to

suggest that an increased risk is currently more marked for those age groups that include a substantial proportion of women actually born in the UK or who would have migrated in their childhood (i.e., the groups studied in the present study) (Eade *et al.*, 1996a; Smith & Prior, 1997; Summerfield & Babb, 2003). In a recent survey of England and Wales, women of South Asian origin aged 20-29 were found to have higher specific breast cancer incidence rates than their non-South Asian counterparts (10.1 compared to 6.7 per 100,000) (Winter *et al.*, 1999). The generational trends in risk factors analysed for the Bangladeshis in this study would seem congruent with these age cohort differentials in incidence rates.

As a whole, these findings prompt a reassessment of South Asian groups as a population at low-risk for breast cancer. They also underline the need for public health programmes designed to promote awareness of and a reduction in breast cancer risk by focusing on those behaviours that are amenable to change. This is particularly relevant considering that breast cancer constitutes the most common type of malignancy among South Asian women (34% of all site cases) (Winter *et al.*, 1999). The hormonal results presented in this dissertation, together with the published evidence of the effects of early life factors on breast cancer risk, suggest that the most effective and possibly long-lasting interventions will be those based on a life course approach. Healthy patterns of diet and exercise from childhood onwards are likely to impact several risk factors for breast cancer simultaneously. Additionally, efforts must be sustained to encourage behaviours that may add protective effects during adult life.

In conclusion, this study illustrates the social and biological transformations taking place in a specific migrant community that are potentially relevant for public health. However, this research has implications beyond the Bangladeshis in London, and may apply to other migrant groups and populations in transition.

APPENDIX A

Socio-demographic Questionnaires

A MIGRATION STUDY OF DEVELOPMENTAL EFFECTS ON REPRODUCTIVE
HORMONE LEVELS
Department of Anthropology, University College London

CONFIDENTIAL

NOTES TO INTERVIEWER:

- Tick in the boxes if appropriate like this (√). If question is not applicable, please cross
the number off.

ID NUMBER   -

Date of interview: /   /
Language of interview
Recruitment place:
Referred by:
Interviewer's initials:
Coded by:

GENERAL QUESTIONNAIRE

♦ *Thank you for taking part in this study. We would like to stress that your answers will
be treated in strict confidence. All the information you provide will be only for statistical
analysis and will NOT be disclosed to third parties. It will not be possible to identify
individuals in any results.*

I. PERSONAL INFORMATION

1.1 What is your full name?

1.2 What is your home address?

1.3 What is your home telephone number?

1.4 Can you give us a permanent address/ telephone where we can locate you if future
follow-up is necessary?

1.5 Do you know your exact date of birth? If so, please give: Day /Month/ Year

1.6 If not, were you born before, on or after Shadinata Judu (1971)?
( ) before
( ) the year of Shadinata Judu
( ) after

If before, what school class where you in during Shadinata Judu?

If after, during which of the following periods were you born?

( ) Mujib Period (1971-1975)
( ) Zia Period (1976-1981)
( ) Ershad Period (1982-1990)

1.7 Where were you born? (Country, City/Village/Town/District)

1.8 Is your birthplace:
( ) a village (rural)
( ) a town/city (urban)

1.9 Did you grow up in a different place than where you were born?
( ) yes
( ) no
If yes, please indicate the place(s) where you grew up (Country,
City/Village/Town/District) and the age at which you moved

1.10 Where was your mother born? (Country, City/Village/Town/District)

_____

1.11 Where was your father born? (Country, City/Village/Town/District)

1.12 What is your marital status?

1.13 If ever married, how old were you when you first got married?

1.14 If married, where was your husband born? (Country, City/Village/Town/District)

1.15 If married, do you live with your in-laws? If not, please specify where

1.16 If married, is this your first or second marriage?

1.17 If married, what is your husband's name?

II. SOCIOECONOMIC INFORMATION

*Please answer the following questions referring to your **current** home.*

2.1 What type of housing do you live in?
( ) house
( ) flat
( ) other, specify

2.2 Does your family own or rent the place you live in?
( ) owns
( ) rents

2.3 If rented, who pays the rent?
( ) family
( ) council
( ) other, please specify

2.4 If rented, who is your landlord?
( ) council/ Local authority
( ) private landlord or letting agency
( ) other, please specify

2.5 How many rooms do you have for use **only** by your family?
Do not count bathrooms and dressing rooms or storage rooms
*Do count all other rooms, for example: kitchens, living rooms, bedrooms and studies. If
two rooms have been converted into one, count them as one room.*

2.6 Does your family/ in-laws have any other property in England?
( ) no
( ) yes, please specify (e.g ancestral home, shop, .building, landed property, etc.)

2.7 Does your family/ in-laws own any property or farm land in Bangladesh?
( ) no
( ) yes, please specify which type (e.g. ancestral home, shop, building, landed property) and where

2.8 In England, does your family (in-laws/ parents) own a car?
( ) no
( ) yes   if yes, please specify who?

2.9 How many members are there *permanently* living in your *current* house?
Please indicate their relationship to you, their ages and their occupation.

Relationship to you	Occupation/job	Age

2.10 What kind of income does your family receive (*current home*)?
( ) Earnings from employment
( ) Earnings from self-employment (service)
( ) Earnings from family business
( ) State retirement pension
( ) Pension from former employer
( ) Child benefit
( ) Job-seekers allowance
( ) Income support
( ) Family credit
( ) Housing benefit
( ) Maintenance benefits
( ) Other state benefits
( ) Interest from savings and investments
( ) Other kinds of regular allowance from outside your household (e.g. student grants, rent)

2.11 If your family has a business, please specify which kind (shops, etc.)

2.12 How long has the family business been going on for?

III. EDUCATION INFORMATION

3.1 Have you ever attended /are you attending school?
( ) yes   If yes, please specify in which country
( ) no

3.2 What is the highest class in school/ college you have completed?

3.3 Do you have any academic qualifications?

( ) yes   If yes, please specify
( ) no

3.4 If presently married, has your husband ever attended school?
( ) yes   If yes, please specify in which country
( ) no

3.5 What is the highest class in school/ college your husband/partner has completed?

3.6 Does he have any academic qualifications?
( ) yes   If yes, please specify
( ) no

3.7 Has your father ever attended school?
( ) yes
( ) no

3.8 What is the highest class in school/college he completed?

3.9 Does he have any academic qualifications?
( ) no
( ) yes   If yes, please specify

3.10 Has your mother ever attended school?
( ) yes
( ) no

3.11 What is the highest class in school/college she completed?

3.12 Does she have any academic qualifications?
( ) no
( ) yes   If yes, please specify

3.13 What is/was your parents first language?

3.14 What is your mother tongue?

3.15 How proficient are you in your **parents'** mother tongue?

	Not at all	A little	Quite good	Fluent
Speaking				
Reading				
Writing				

3.16 How proficient are you in English?

	Not at all	A little	Quite good	Fluent
Speaking				
Reading				
Writing				

3.17 What language do you usually speak at home with your husband or other adults in the house?
( ) mainly English
( ) mainly mother tongue
( ) English and mother tongue equally
( ) other language, please specify

3.18 What language do you speak at home with your children?
( ) mainly English

( ) mainly mother tongue
( ) English and mother tongue equally
( ) other language, please specify

3.19 Did you speak any English before coming to Britain?
( ) yes
( ) no

IV. EMPLOYMENT INFORMATION

4.1 Have you **ever** had a job?
( ) yes
( ) no

4.2 Have you ever worked from home (e.g. dressmaking, etc.)?
( ) yes, please specify
( ) no

4.3 What is your current occupation? *Include self-employment, volunteer work, housewife.*

4.4 If presently married, what is your husband's occupation?

4.5 What is/was your father's occupation?

4.6 What is/was your mother's occupation?

V. MIGRATION

5.1 When did you move from Bangladesh to England permanently?

5.2 How old were you when you moved permanently to England from Bangladesh?

5.3 Where did you live in Bangladesh **before** coming to the England (City/Village/Town/District)? If you lived in various places, please state in chronological order and state how old you were then

5.4 Is that place:
( ) a village (rural)
( ) a town/city (urban)

5.5 What was your occupation in Bangladesh before coming to England?

5.6 If you were married before coming to England, what was your husband's occupation in Bangladesh?

5.7 What was the purpose of your migration from Bangladesh to England?
( ) economic
( ) education
( ) accompany family
( ) marriage
( ) other specify

5.8 Who moved together with you at the time of migration?
( ) husband
( ) father
( ) mother
( ) sister/ brother
( ) children
( ) father/ mother in law

( ) sister/brother in law
( ) son/daughter in law
( ) other family members

5.9 Where did you live when first arriving England? (city/town)

5.10 What was your occupation when first arriving in England?

5.11 What was your parent's/husband's occupation when first arriving in England?

5.12 If you were born in the UK of Bangladeshi parents, in which year did **they** arrive in England?
Father_____ ( ) Don't know
Mother_____ ( ) Don't know

5.13 Where did they live in Bangladesh **before** coming to the England (City/Village/Town/District)?

5.14 What was your family occupation in Bangladesh before coming to England?

5.15 What was the purpose of your parents' migration from Bangladesh to England?

5.16 Is/are there any other member(s) of your family living in England?
( ) yes
( ) no

If yes, please specify:

Relative (include in-laws, cousins, etc)	What is his/her occupation?	How long has been in England for?	Where do they live in England?

5.17 Is/are there any other member(s) of your family living in Bangladesh?
( ) yes
( ) no

If yes, please specify:

Relative (include in-laws, cousins, etc)	What is his/her occupation?	Where do they live in Bangladesh?

5.18 Does your family keep any business in Bangladesh? If yes, please specify

VI. PHYSICAL ACTIVITY

6.1 Do you practice any sport/ do any exercise?
( ) yes   If yes, how often (times/week)?
( ) no

6.2 If yes, which type?

6.3 Do you walk continuously for more than 20 min on a daily basis?
( ) yes
( ) no

6.4 Do you have household help?
( ) yes, please specify
( ) no

6.5 Do you do any type of household work?
( ) yes, please specify
( ) no

VII. GENERAL HEALTH

7.1 Do you have any long-term illness, health problem or disability which limits your daily activities or the work you can do?
( ) yes   If yes, please specify
( ) no

7.2 When was your last visit to a doctor?

7.3 Do you attend a private or public doctor/clinic?

7.4 Have you had any illnesses in the last 6 months?
( ) yes If yes, what kind?
( ) no

7.5 Have you had intestinal worms or amoebas in the past 6 months?
( ) yes   If yes, please specify?
( ) no

7.6 Do you suffer from any of these diseases?

Diabetes	( ) yes ( ) no ( ) don't know
Heart disease	( ) yes ( ) no ( ) don't know
High cholesterol	( ) yes ( ) no ( ) don't know
High blood pressure	( ) yes ( ) no ( ) don't know
Anaemias	( ) yes ( ) no ( ) don't know
Arthritis or rheumatism	( ) yes ( ) no ( ) don't know
Other (please specify)	( ) yes ( ) no ( ) don't know

7.7 Is there any history of diabetes in your family?
( ) yes, if yes please specify who?
( ) no
( ) don't know

7.8 Is there any history of high blood pressure in your family?
( ) yes, if yes please specify who?
( ) no
( ) don't know

7.9 Is there any history of heart disease in your family?
( ) yes, if yes please specify who?
( ) no
( ) don't know

7.10 Has any member of your family had a bone fracture?
( ) yes, if yes please specify who and which type?
( ) no
( ) don't know

7.11 Does anyone of your female relatives have a humpback?
( ) yes, if yes please specify who?

( ) no
( ) don't know

7.12 Is there any history of cancer in your family?
( ) yes
( ) no
( ) don't know
If yes, please specify which member of your close family has been affected and by which kind

7.13 Have you had any operations?
( ) yes, please specify
( ) no

7.14 Are you a vegetarian?
( ) yes
( ) no

If yes please specify what type:
( ) vegan (no animal products)
( ) lacto-ovo vegetarian (no meat, fish, chicken, etc.)
( ) other, please specify

7.15 Have you been on a special diet in the last 3 months?
( ) no
( ) yes, to lose weight
( ) yes, to gain weight
( ) yes, low fat
( ) yes, low sugar
( ) yes, high fibre
( ) yes, other, please specify the kind of diet and the reason

7.16 Have you lost or gained weight in the past 3 months?
( ) yes, please specify
( ) no

7.17 Is your weight substantially different from before you had your children?
( ) yes   If yes, higher or lower?
( ) no
( ) not applicable

7.18 Do you regularly take any nutritional supplements, vitamins or minerals?
( ) yes If yes, please specify what kind
( ) no

7.19 Have you taken any medications during the past month?
( ) yes
( ) no
If yes, how many kinds (including homeopathy/kabiraji)

Name of medicine	Have you taken this medicine in the last 2 weeks? Yes/No
1	
2	
3	

7.20 Do you smoke tobacco?
( ) yes
( ) no

VIII. REPRODUCTIVE HISTORY INFORMATION

8.1 How old were you at your first menstruation? State whether it is an exact age or an approximation.
( ) exact
( ) approximation

8.2 Which school class where you in when you had your first period (if applicable)?

8.3 When did your last period **start**?
( ) day ( ) month

8.4 How long does the bleeding normally last?

8.5 Have you ever been pregnant?
( ) yes
( ) no

8.6 How old were you when you were pregnant for the first time?

8.7 *Now I would like to ask you about all the pregnancies that you ever had so far.*

No	Year	Pregnancy type (live birth, miscarriage, stillbirth, clinical abortion, ectopic)	Live birth but premature (how many weeks?)	Sex	Age	Place of birth (Home birth/ hospital /clinic) (private /state)	Country of birth	Birth-weight	Breast-fed? (yes/no)	Duration of breast-feeding (months)
1										
2										
3										
4										
5										
6										

8.9 Have you had problems getting pregnant?
( ) yes
( ) no

8.10 Have you ever been diagnosed with any genital infections?
( ) yes   If yes, specify
( ) no

8.11 Have any of your daughters had their first period?
( ) yes   If yes, how old were they?
( ) no
( ) don't know

8.12 Do you know how old was your mother when she had her first period?
( ) yes   If yes, please indicate _____ years
( ) no

8.13 Do you know how old was your mother when her periods stopped completely?
( ) do not know
( ) yes, please indicate _____ years
( ) have not stopped and she is _____ years old

8.14 Were **you** born:
( ) at home
( ) at a hospital/clinic
If born at a hospital/clinic, please state the name and place (city/town) and if private/public

8.15 Were you born prematurely?
( ) yes   If yes, how many weeks
( ) no
( ) do not know

8.16 Do you know your birth weight?
( ) yes   If yes, please indicate
( ) no

IX. SOCIAL AND LEISURE ACTIVITIES

9.1 What ethnic background do **most** of your friends in England have?
( ) Bangladeshis
( ) Pakistanis
( ) Indians
( ) English
( ) Black
( ) Chinese
( ) other, please specify

9.2 Do you ever eat meals in an English (White) home?
( ) yes   If yes, how often?
( ) no

9.3 How often do you have tea/ meals over at relative's/friend's homes?

9.4 What do you commonly do for recreation in your free time?

♦ Thank you very much for your participation
and support in helping us with this study. If
there is anything further you would like to add
or comment upon please let us know.

ANTHROPOMETRY

♦ *We would like to take some measurements of your height, weight and skinfolds.*

ID NUMBER   -
Date when measurements where taken: /   /
Researcher's initials

	1st reading	2nd reading
Height (cm)		
Sitting height (cm)		
Weight (kg)		
Mid-arm circumference (mm)		
Subscapular skinfold		
Biceps skinfold		
Triceps skinfold		

Comments/Observations

APPENDIX B

Food Questionnaires

A MIGRATION STUDY OF DEVELOPMENTAL EFFECTS ON REPRODUCTIVE HORMONE LEVELS

Department of Anthropology, University College London

CONFIDENTIAL

NOTES TO INTERVIEWER:

- Tick in the boxes if appropriate like this (√) If the question is not applicable, please cross the number off.

ID NUMBER   -

Date of interview: /   /
Language of interview:
Recruitment place:
Refered by:
Interviewer's initials:
Coded by:

FOOD HABITS QUESTIONNAIRE

♦ *Thank you for agreeing to take part in this survey. The following questions relate to your usual eating habits. Please answer all the questions as fully as you can. The information will be held in strict confidence.*

I. FOODWAYS

1.1 How many meals do you normally eat a day?

1.2 How many tea/snack breaks do you normally have a day?

· 1.3 Do you ever eat foods **bought** frozen? (eg. Vegetables, fish, meat, fruit)
( ) yes
( ) no

If yes, what type and how often?

Type of food	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.4 Do you ever eat tinned food?
( ) yes
( ) no

If yes, what type and how often?

Type of food	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.5 Do you ever eat ready-made meals (packaged) (e.g. quiche, pies, lasagne, etc.)?
( ) yes
( ) no

If yes, what type and how often?

Type of food	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.6 Which of the following do you cook and how often?

Food type	Daily	Weekly/fortnightly	Monthly	Only on special occasions	Never
Main meals- Asian					
Main meals- English					

1.7 Do you consume any foods imported from Bangladesh? (p.e. fish, vegetables, fruit).
State whether fresh or frozen
( ) yes
( ) no

If yes, what type and how often?

Type of food	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.8 Are there any foods that you buy/prepare because your children like them (if applicable)?
( ) yes
( ) no

If yes, what type and how often?

Type of food	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.9 How often do you eat food out or buy food to "take away"?

Type of place	Daily	Weekly/Fortnightly	Monthly	Less than once a month	Never

1.10 Do you usually do most of the shopping for food?
( ) yes
( ) yes, with another member of the family
( ) no, if not please specify who does

1.11 Where does the shopping is normally done?
( ) supermarket
( ) street market/ stalls
( ) halal butcher
( ) non-halal butcher
( ) asian store/cash and carry
( ) other, please specify

II. FOOD CHANGES

If you migrated from Bangladesh:

2.1 Which foods do you eat **more** in England than when you lived in Bangladesh?

2.2 Which foods do you eat **less** in England than when you lived in Bangladesh?

III. SEMI-QUANTITATIVE FOOD FREQUENCY QUESTIONNAIRE

♦ *We would now like to ask you about some foods which you may eat.*

3.1 Do you eat roti/chapatti/porotha/naan?
( ) yes
( ) no

3.2 Do you eat bread?
( ) yes
( ) no

3.3 If yes, which type of bread do you eat?
( ) white
( ) brown
( ) wholemeal

3.4 About how many pieces of bread/roti/chapatti/naan do you eat on a usual day?
( ) 5 or more a day
( ) 1 to 2 a day
( ) none

3.5 What do you normally eat for breakfast?
( ) tea and biscuits
( ) chapatti/porotha and savoury dish
( ) cereal or porridge

3.6 Do you normally take Nasta afterwards?
( ) yes
( ) no

3.7 How often, on average, do you eat rice?
( ) with every meal
( ) twice daily
( ) once a day
( ) 2-3 times/week
( ) less than once/week
( ) Rarely or never

3.8 How often, on average, do you eat noodles/pasta?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) less than once/week
( ) Rarely or never

3.9 How often, on average, do you prepare dishes made from other grains such as millets, semolina, cornmeal, rice flour?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.10 Excluding chips and crisps, how often on average do you eat potatoes?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.11 How often, on average, do you eat lentils (dhals)?
( ) with every meal
( ) twice daily
( ) once a day
( ) 2-3 times/week
( ) less than once/week
( ) Rarely or never

3.12 How often, on average, do you eat other pulses (peas, beans, including baked beans)?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.13 How often on average, do you eat cooked vegetables?
( ) with every meal
( ) twice daily
( ) once a day
( ) 2-3 times/week
( ) less than once/week
( ) Rarely or never

3.14 How often on average do you eat salad? Please specify if green or other.
( ) with every meal
( ) twice daily
( ) once a day
( ) 2-3 times/week
( ) less than once/week

( ) Rarely or never

3.15 How often, on average, do you eat fruit or real freshly squeezed natural fruit juice?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.16 How often, on average, do you drink tinned or packed fruit juice?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.17 How often, on average, do you eat cheese?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.18 Which type of cheese do you eat most frequently? (paneer, cheddar, parmesan, etc.

3.19 How often do you eat any other dairy produce (yoghurt/curd/lassi/lachi/shomai/sourcream)?
( ) with every meal
( ) twice daily
( ) once a day
( ) 2-3 times/week
( ) less than once/week
( ) Rarely or never

3.20 How often, on average, do you eat chicken or turkey? Please circle the one you eat most.
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.21 How often on average, do you eat red meet (beef or lamb)? Please circle the one you eat most.
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.22 How often, on average, do you eat any fried food, including fried fish or chicken, chips, fried rice, puris, bhajis)?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.23 Apart from fried fish, how often, on average do you eat fish curry or seafood?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.24 How often, on average, do you eat eggs?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.25 How often, on average, do you eat sweet or savoury snacks such as: chocolates, crisps, nuts or biscuits? Include: savoury biscuits such as muri, chanachur, Bombai mix, etc.
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.26 How often, on average, do you eat a serving of cakes, pies, puddings, pastries, Indian sweets?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.27 What sort of fat do you usually use for cooking or frying food?
( ) butter
( ) ghee
( ) hard or soft margarine
( ) Soyabean, olive, palm, mustard, sunflower, corn, coconut
( ) solid cow's fat
( ) do not use oil or fat in cooking
( ) other, please specify

3.28 During mealtimes, what do you normally drink?
( ) water
( ) freshly squeezed fruit juice
( ) tinned or packed fruit juice
( ) sodas (e.g. Coca cola, Pepsi lemonade)
( ) other, please specify

3.29 How often do you drink sodas (e.g. Coca cola, Pepsi, lemonade)?
( ) daily
( ) 4 to 3 times/week
( ) 1 to 2 times/week
( ) Less than once/week
( ) Rarely or never

3.30 Do you drink milk?
( ) yes
( ) no

3.31 What kind of milk do you drink?
( ) cow milk

( ) goat milk
( ) soya milk
( ) other, please specify

3.32 Is the milk:
( ) whole
( ) semi-skimmed
( ) skimmed

3.33 Do you drink?
tea   yes ( ) no ( )
coffee   yes ( ) no ( )
other ( ), please specify

3.34 Do you add sugar to:
tea   yes ( ) no ( )
coffee   yes ( ) no ( )

If yes, how many spoonfuls?

3.35 Do you add milk to:
tea   yes ( ) no ( )
coffee   yes ( ) no ( )

3.36 Has salt been generally added to your food during cooking?
( ) yes (include sea salt/iodine salt)
( ) no, do not use salt in cooking
( ) use "Low-salt" or salt alternative

3.37 Do you often eat the same menu for dinner as for lunch (leftovers)?
( ) yes
( ) no

Observations/Comments:

♦ *Thank you very much for your participation.*

APPENDIX C

Anthropometric measurements

Women were weighed and measured at the end of their participation in the study. Skinfold thickness and Body Mass Index (BMI) were used to assess current energy status in the form of relative body fat. Anthropometric measurements were taken following standard procedures Gibson (1990).

Height

Height was measured using a portable stadiometer marked with a metric measuring scale. Participants were asked to remove shoes. Measurements were taken with the participant stretching to the maximum height and the head positioned in the Frankfort plane. Two readings were taken to the nearest millimetre and the average reported.

Weight

Weight was measured, using a portable electronic scale with a digital display. Participants were asked to remove shoes and any bulky clothing. Two consecutive measurements were recorded to the nearest 100 g and the average reported.

Triceps skinfold thickness

Triceps skinfold thickness was measured at the posterior side of the arm, over the triceps muscle, at the previously marked midpoint of the right upper arm using a Harpenden skinfold calliper.

With the participant standing and with the right arm hanging loosely by her side, the investigator grasped a vertical pinch of skin and subcutaneous fat between thumb and forefinger about 1 cm above the previously marked midpoint. Pulling the skinfold gently away from

underlying muscle, the skinfold calliper was placed on the skinfold at the midpoint marked. Two successive readings were taken, while maintaining a grasp of the skinfold, and the average recorded to the nearest mm. Each reading was taken as soon as the jaws of the calliper came into contact with the skin and the dial reading stabilised.

Body Mass Index (BMI)

Body Mass Index (BMI) was calculated for participants for whom a valid height and weight measurements were available as weight (kg)/ height (m^2) and grouped as follows:

20 or less	Underweight
20 to 25	Desirable
25 to 30	Overweight
Over 30	Obese

Classification WHO, International Obesity Task Force, Geneva (1998).

APPENDIX D

Steroid radioimmunoassays

Protocols for direct salivary progesterone and oestradiol immunoassay as described in Lu *et al.* (1997, 1999).

Direct salivary progesterone radiommunoassay

A competitive equilibrium for specific antibody sites is established between standards of progesterone and antibody and [1,2,6,7-^{3}H-progesterone] in pH 7.56 PBS-BSA-EDTA buffer. Unbound 3H-progesterone is separated by addition of dextran-coated charcoal.

Materials:

A. PBS-BSA-EDTA Buffer (0.1 M NaH$_2$PO$_4$ pH 7.56)

13.8 g NaH$_2$PO$_4$ •H$_2$0

8.7 g NaCl

1.05 g BSA

0.56 g EDTA

0.1 g Thimerosal

Add to 1000 ml distilled water. Adjust pH to 7.56 with NaOH.

B. "Modified" Steroid Buffer (0.1 M phosphate pH 6.95)

4.0 g NaH$_2$PO$_4$ •H$_2$0

9.0 g NaCl

11.0 g NaH$_2$PO$_4$ (extracted for E$_2$ assay)

1.0 g Sodium Azide

1.0 g Gelatin

1000 ml Distilled water

Gelatin is first dissolved in 100 ml of water heated on a hot-plate. When cool, add 800 ml of water, add other ingredients, bring pH to 6.95, and bring volume to 1000 ml.

C. Antiserum

Antiserum prepared at Dr. Chatterton's laboratory in Northwestern University Medical School is used at a dilution of 5000. The antiserum cross reacts 12.12% with 5β-pregnanedione, 5.5% with 5α-pregnanedione, 4.22% with deoxycorticosterone, 1.56% with 20-β-OH-P, 2.32% with 5β-pregnenolone, 1.6% with corticosterone, 0.55% with pregnenolone, and <0.1% with 20-α-OH-P.

D. Tracer

$[1,2,6,7-^3H$-progesterone$]$ is used at a concentration of 10,000 cpm/0.1 ml in the assay tube.

E. Stripped Saliva (for Quality Control tubes)

Quality control pools were prepared from saliva collected from women volunteers during the early to midfollicular phases of their cycles and from women in midpregnancy.

Add 5 g BDH Agarose in 100 ml distilled water and heat to 70° C with constant stirring until it is dissolved completely. Then add 20 g charcoal when the solution cools to 50°C and pour into 200 ml acetone with vigorous stirring. Filter the charcoal through a Buchner funnel and dry overnight at 37° C. Break up lumps and keep in a well sealed container. 1 g Agarose-charcoal is added to 40 ml saliva and mixed (by shaker) overnight at room temperature and centrifuged to remove the charcoal.

F. Standards

Progesterone is obtained from Sigma Chemical Company, St. Louis, MO. A stock solution of 1.0 mg/ml is prepared in methanol and stored

sealed in the cold room. Standards are made in steroid buffer S6 to S1 (stepwise dilutions).

Standard	Dose
NSB	100 ng/ml
S6	1 ng/ml
S5	0.5 ng/ml
S4	0.25 ng/ml
S3	0.125 ng/ml
S2	0.0625 ng/ml
S1	0.032 ng/ml

G. Dextran-coated charcoal (DCC)

Add 0.05 g of dextran to 100 ml of Steroid Buffer. Allow 20 minutes to stir and dissolve. Add 0.5 g of activated charcoal (Sigma). Stir for one hour at room temperature. Store in cold room and add at 4°C to the samples. Prepare fresh DCC every other week.

H. Sample preparation

Saliva samples are stored in the –20°C freezer upon arrival to the lab. They are thawed, centrifuged at 1500 x g for an hour and the supernatant used for analysis. Samples were assayed without extraction.

Only the samples corresponding to the last 18 days of each individual menstrual cycle were included in the progesterone assay. This was meant to exclude most of the follicular phase during which progesterone levels are below sensitivity of the assay.

Assay procedure:

Add 200 µl of standards, steroid buffer (for total counts "T" and zero "Bo" tubes), or saliva samples to labelled disposable tubes, labelling the

tubes as follows: T, NSB (non-specific binding), Bo, S1...S6, QC, samples, QC. Everything is run in duplicate.

With a repeater dispenser add 100 μl PBS-BSA-EDTA solution containing the 3H-P4 and P4-AS to each tube. The volume in the assay is now 300 μl.

Incubate on the shaker at room temperature for 3 hours and then place in the cold room for at least one hour (or overnight).

In the cold room, add 200 μl of DCC to all tubes except "T" tubes (add 200 μl steroid buffer to the "T" tubes). The DCC should be stirred 10 minutes before and continuously while dispensing.

Mix the assay tubes on the rotary shaker in the cold room for 10 minutes. Centrifuge for ten minutes at full speed in the Beckman table-top centrifuge in the cold room.

Remove 280 μl and add 3.5 ml of scintillation fluid with the mictomedic pipettor-dilutor. (The display should read 38, 70). Do not allow the assay tubes to remain at room temperature for more than 5 minutes before removing an aliquot for counting. (The other centrifuge carriers containing samples can be stored in the lab refrigerator). Count for 2 minutes using the appropriate dilution and standard set with the protocol salivap4.

Calculations:

Data reduction is carried out by the Iso-Data program of the counter. NSB is subtracted from each count and the result is divided by the total to determine the percent binding. The count data is converted to % bound (100 x count – NSB) / Bo and is plotted on a linear logit-log scale. Unknowns are calculated from the linear standard curve.

Direct salivary oestradiol radioimmunoassay

Salivary oestradiol (E_2) concentrations were measured with the use of a double-antibody radioimmunoassay (RIA) with $[I^{125}]E_2$.

Materials:

A. "Modified" Steroid Buffer (0.1 M phosphate pH 6.95)

B. Tracer and antiserum

Were obtained from Diagnostic Services Laboratories (Webster, TX). The antiserum cross-reacts 2.4% with oestrone, 0.01% with oestrone sulfate, 0.21% with 16-ketooestradiol, 2.56% with oestradiol 3-glucuronide, 0.64% with oestriol, and <0.1% with nonphenolic steroids tested.

The total $[I^{125}]E_2$ per tube was approximately 15,000 cpm. Antiserum is diluted to give approximately 40% binding.

C. 5.5% NRS (Non-rabbit serum)

5.5 ml NRS

91 ml steroid buffer

D. Precipitating buffer

Prepared by titrating the amount of sheep antirabbit gamma-globulin (SARGG) required for the precipitation of 0.1 ml of 9% normal rabbit-antiserum.

4.5 SARGG

4.8 g polyethylene glycol (PEG)

90 ml steroid buffer

E. Stripped Saliva (for Quality Control tubes)

F. Standards

Pure E_2 for standards is obtained from Sigma Chemical Co. (St. Louis, MO).

An E_2 stock solution of 1.0 µg/ml is prepared in methanol and stored sealed in the cold room. Standards are made in Steroid Buffer S8 to S1 (stepwise dilutions).

Standard	Dose
S8	200 pg/ml
S7	100 pg/ml
S6	50 pg/ml
S5	25 pg/ml
S4	12.5 pg/ml
S3	6.25 pg/ml
S2	3.125 pg/ml
S1	1.56 pg/ml

G. Sample preparation

Saliva samples are stored in the –20°C freezer upon arrival to the lab. They are thawed, centrifuged at 1500 x g for an hour and the supernatant used for analysis. Samples were assayed without extraction.

All samples in each individual menstrual cycle were included in the oestradiol assay.

Assay procedure:

Label disposable tubes as follows: T, NSB, Bo, S1...S6, QC, samples, QC. Everything is run in duplicate.

Add 500 µl of steroid buffer to NSB tubes, and 400 µl to Bo. Add 400 µl of standards and saliva samples.

With a repeater dispenser add 100 µl of E_2 antibody (1:2) diluted in steroid buffer to all tubes except "NSB" and "T" tubes. The volume in the assay is now 500 µl.

Vortex all tubes, incubate on the shaker at room temperature for 1 hour.

Add 25 µl of E2 I^{125} reagent to each tube including "T" tube.

Vortex all tubes, incubate on the shaker at room temperature for 2 hour.

Add 100 µl of 5.5% Non-rabbit serum (NRS) and 1ml of precipitating buffer to all tubes except " T" tube. Vortex and shake at room temperature for 15 or 20 minutes.

Centrifuge all tubes, except "T" tube for 15-20 minutes at 1500 x g.

Decant all tubes, except " T" tube by simultaneous inversion with a sponge rack into radioactive waste receptacle. Allow them to drain on absorbent material for 15-30 seconds and gently blot the tubes to remove any droplets adhering to the rim before returning them to the upright position. Failure to blot the tubes adequately may result in erroneous and non-reproducible results. Count all tubes in the gamma scintillation spectrometer for one minute.

Calculations:

Data reduction is carried out by the E$_2$ programme of the counter. Same protocol as for progesterone.

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